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THE RENAL REGULATION OF ACID BASE BALANCE WITH SPECIAL REFERENCE TO THE MECHANISM FOR ACIDIFYING THE URINE[1]

By Dr. ROBERT F. PITTS

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LARGE quantities of acid are continuously produced in the body by the metabolism of the various foodstuffs, yet in health the hydrogen ion concentration of the body fluids is maintained remarkably constant. This regulation of balance between the acidic and basic constituents of the body fluids is dependent upon both respiratory and renal homeostatic mechanisms. In a quantitative sense the rate of production of carbonic acid, amounting to about 20 mols per day, far exceeds the rate of production of other metabolic acids. But because of the volatility of its anhydride, carbon dioxide, carbonic acid is readily and rapidly eliminated by the lungs. Less than one one-hundredth of this quantity of phosphoric and sulfuric acid is produced each day, yet the excretion of these acids, which is effected largely by the kidneys, is in some ways a greater problem than is the excretion of the much larger quantities of carbonic acid. Rarely does any disease process lead to a disturbance of acid base balance because it interferes with the elimination of carbon dioxide in the lungs.

[1] Presented as an Abraham Flexner Lecture at Vanderbilt University School of Medicine on April 20, 1945, and as a Lecture in Medicine at the University of Utah School of Medicine on May 18, 1945.

In contrast at least two disease processes lead to disturbances of acid base balance because they interfere with the adequate elimination of acid by the kidneys. Thus in severe uncontrolled diabetes the excessive metabolic production of beta-hydroxybutyric and acetoacetic acid so overwhelms the normal renal mechanisms for excretion of acid that acidosis results. On the other hand in chronic diffuse glomerulonephritis the kidneys are so damaged that their reduced capacity to excrete acid is inadequate to cope with the normal metabolic production of sulfuric and phosphoric acid, and acidosis results.

In this lecture I propose first, to review briefly the contribution of the renal acid excreting mechanisms to the regulation of acid base balance; second, to present some recent experiments[2] designed to elucidate the nature of the mechanism for acidifying the urine; and third, to point out how the inadequate functioning of these mechanisms in diabetes and in chronic renal disease leads to the development of clinical acidosis.

Let us first review briefly the quantitative aspects of the renal excretion of acid in the normal healthy adult. In the metabolism of 100 gm of protein and 100 gm of fat the normal individual produces phosphoric and sulfuric acid in amounts equivalent to 1,500 cc of N/10 acid. The average diet contains enough available base to neutralize about half of this acid. The remaining half must be neutralized by base derived from bicarbonate of the body fluids. If this excess acid were excreted as neutral sodium salts, the body stores of available base would be rapidly depleted. Accordingly two renal mechanisms have been developed for the excretion of acid without the loss of equivalent amounts of fixed base. First, the renal tubules synthesize ammonia, and convert the sodium salts of the glomerular filtrate into ammonium salts. An equivalent amount of sodium is retained in the body. Second, the renal tubules convert the slightly alkaline glomerular filtrate into an acid urine, and because the acids are excreted partly in the free form, base is retained in the body.

The most acid urine which the kidney can elaborate has a pH of 4.8. At this pH only insignificant amounts of strong acids such as sulfuric and hydrochloric can exist in free form. Hence conservation of base in the excretion of these strong acid anions must be brought about by the conversion of their sodium salts to ammonium salts. But weak acids such as phosphoric, uric and beta-hydroxybutyric can exist in considerable proportion in free form in urine of pH 4.8. Hence conservation of base in the excretion of these weak acid anions can be brought about by the acidification of the urine.

[2] The data summarized in this paper are presented in detail in the *Am. Jour. Physiol.*, 144: 239, 1945.

TABLE 1

MECHANISMS BY WHICH ACID IS EXCRETED WITHOUT LOSS OF EQUIVALENT AMOUNTS OF FIXED BASE. SUMMARY OF QUANTITATIVE DATA ON MAN

	cc N/10 acid/day	Ratio $\frac{NH_3}{acid}$
Normal man:		
1. Excretion of acid combined with NH_3	300–500	1–2.5
2. Excretion of titratable acid	100–300	
Diabetic acidosis:		
1. Excretion of acid combined with NH_3	3,000–5,000	1–2.5
2. Excretion of titratable acid	700–1,500	
Nephritic acidosis:		
1. Excretion of acid combined with NH_3	5–150	0.2–1.5
2. Excretion of titratable acid	20–200	

As is shown in Table 1, compounded from studies of Peters and Van Slyke,[3] Gamble[4] and others, a normal individual excretes the equivalent of 300 to 500 cc of N/10 acid each day in combination with ammonia and 100 to 300 cc as free titratable acid. This titratable acid is largely phosphoric in the form of monobasic phosphate.

The uncontrolled diabetic produces much more metabolic acid than does the normal individual. Not only does he produce phosphoric and sulfuric acids but in addition he produces the ketone bodies beta-hydroxybutyric and acetoacetic acid in extremely large amounts. Total acid production may amount to the equivalent of 5,000 to 10,000 cc of N/10 acid per day. Accordingly the excretion of acid combined with ammonia and the excretion of free titratable acid are greatly increased, as is shown in this table. But despite this tremendous increase in the excretion of ammonia and titratable acid, the renal elimination of acid fails to keep pace with the metabolic production of acid. Ketone bodies are excreted in part as neutral sodium salts and the alkali reserve of the body is depleted.

In nephritis the production of metabolic acid is within normal limits, but the capacity of the kidneys to eliminate acid without loss of base is reduced. As is shown in this table, the ability of the diseased kidney to form ammonia and to acidify the urine is less than that of the normal kidney. The more long standing and severe the disease process the greater is the reduction in functional renal capacity. If the nephritic patient continues to produce some 400 to

[3] J. P. Peters and D. D. Van Slyke, "Quantitative Clinical Chemistry." Vol. 1, "Interpretations." Baltimore: Williams and Wilkins Co. 1932.

[4] J. L. Gamble, "Chemical Anatomy, Physiology and Pathology of Extracellular Fluid." A lecture syllabus. Department of Pediatrics, Harvard Medical School, Boston, 1941.

800 cc of N/10 acid per day in excess of the daily intake of available base, yet is incapable of excreting this excess as free acid and as acid combined with ammonia, it is obvious that his body stores of available base will be rapidly exhausted. In fact in the terminal stages of nephritis the total excretion of acid may drop to 25 cc per day, 5 cc combined with ammonia and 20 cc as free titratable acid. Under conditions such as these the alkali reserve of the body could be exhausted in less than one week.

In the absence of renal disease, both in the normal individual and in the uncontrolled diabetic, the quantity of acid excreted in combination with ammonia exceeds that excreted as free titratable acid. Thus the ratio of ammonia to titratable acid varies between limits of 1 and 2.5 (*c.f.* Table 1). In chronic renal disease the capacity of the kidney to excrete ammonia is reduced to a greater extent than is the capacity to excrete an acid urine. Thus the ratio of ammonia to titratable acid decreases. Terminally in some instances the ratio may return toward normal, not as a result of any increase in ammonia excretion, but as a result of extreme depression of the elimination of free acid.

is secreted into the urine, but some leaks out into the renal venous blood.

The nature of the precursor of ammonia has, in the past, been a subject for considerable controversy. Recently, however, ingenious experiments of Dr. Van Slyke and his associates[6] have demonstrated conclusively that 60 per cent. or more of the urinary ammonia is derived from plasma glutamine, and 40 per cent. or less is derived from plasma amino acid. The kidney contains an enzyme, glutaminase, which rapidly splits off the amide nitrogen of glutamine to form glutamic acid and ammonia. This reaction is illustrated in Table 2. Another enzyme, amino acid oxidase, brings about the oxidative deamination of amino acids to form corresponding keto acids and ammonia. In this table alanine is used as an example, although presumably any amino acid could serve as the precursor of ammonia.

The nature of the renal mechanism for acidifying the urine is less well understood than is that for excretion of ammonia, and has never been subjected to any critical experimental study. It is generally conceded that some process is involved such as that illustrated in the equation at the bottom of Table 2. Thus

TABLE 2

RENAL REACTIONS INVOLVED IN THE SECRETION OF AMMONIA AND IN THE ACIDIFICATION OF THE URINE

Ammonia secretion

1. Glutamine $HOOC \cdot CH(NH_2) \cdot CH_2 \cdot CH_2 \cdot CO(NH_2) + H_2O \longrightarrow$ Glutamic Acid $HOOC \cdot CH(NH_2) \cdot CH_2 \cdot CH_2 \cdot COOH +$ Ammonia NH_3
(*Renal Glutaminase*)

2. Alanine $HOOC \cdot CH(NH_2) \cdot CH_3 + O \longrightarrow$ Pyruvic Acid $HOOC \cdot CO \cdot CH_3 +$ Ammonia NH_3
(*Renal Amino Acid Oxidase*)

Acidification of urine

3. *Dibasic Phosphate* Na_2HPO_4 + *Carbonic Acid* $H_2CO_3 \longrightarrow$ *Monobasic Phosphate* NaH_2PO_4 (Excreted) + *Bicarbonate* $NaHCO_3$ (Reabsorbed)

Let us consider the known facts concerning the renal mechanisms for ammonia excretion and for acidifying the urine. In 1921 Nash and Benedict[5] demonstrated quite simply that the renal tubular cells synthesize ammonia and secrete it into the tubular lumen. Thus they observed that the concentration of ammonia in the arterial blood is vanishingly low; that the blood ammonia is unchanged in acidosis when the excretion of ammonia is much increased; and that the quantity of ammonia excreted far exceeds the quantity filtered through the glomeruli. Furthermore, the concentration of ammonia in the blood leaving the kidney is always higher than that in the blood entering the kidney. Therefore it is apparent that ammonia must be formed in the kidney from some precursor in the arterial blood. Most of this ammonia carbonic acid reacting with dibasic phosphate forms monobasic phosphate and sodium bicarbonate. Base is conserved by the reabsorption of sodium bicarbonate and free titratable acid is excreted in the urine in the form of monobasic phosphate. Although this reaction adequately describes the end result of urinary acidification, it does not indicate the means by which this end is achieved. Indeed three distinct theoretical mechanisms have been postulated, each based fundamentally upon this reaction.

In Fig. 1 the three current theories as to the nature of the mechanism for acidifying the urine are illustrated in highly diagrammatic fashion. The kidney is represented as a single renal unit composed of glomerulus and tubule. Such a simplified representation

[5] T. P. Nash and S. R. Benedict, *Jour. Biol. Chem.* 48: 463, 1921.

[6] D. D. Van Slyke, R. A. Phillips, P. B. Hamilton, R. M. Archibald, P. H. Futcher and A. Hiller, *Jour. Biol. Chem.*, 150: 481, 1943.

is permissible for the million or so nephrons comprising each kidney are functionally identical in a qualitative sense. In each glomerulus there is formed an ultrafiltrable of plasma; the pH of the filtrate is the same as that of the plasma, namely, pH 7.4. In its passage down the tubule this filtrate is elaborated into acid urine of pH 4.8 or higher.

According to the *phosphate reabsorption theory* the significant constituents of the glomerular filtrate are monobasic and dibasic phosphate, present in the original filtrate in a ratio of 1 part of the monobasic salt to 4 parts of the diabasic salt. It is presumed that

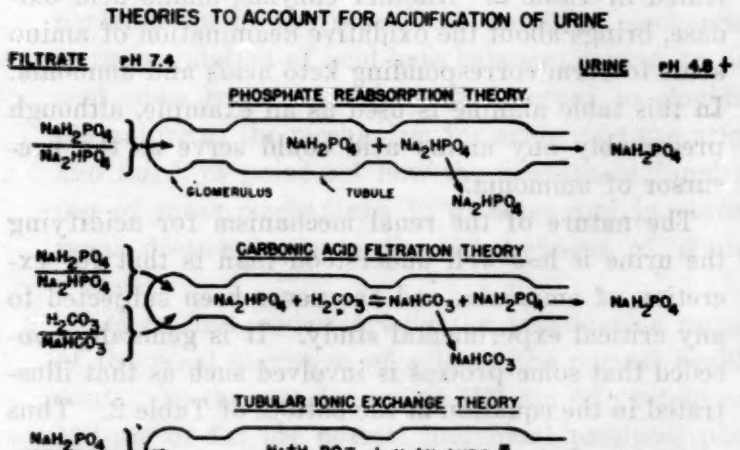

FIG. 1. From Pitts, R. F. and Alexander, R. S., *Amer. Jour. Physiol.*, 144: 239, 1945.

the diabasic phosphate is reabsorbed by the renal tubules and returned to the postglomerular blood, whereas the monobasic phosphate is excreted and constitutes the titratable acid of the urine. If the urine contained only monobasic phosphate it would have a pH of approximately 4.8, and for each millimol of phosphate excreted 8/10th of a milliequivalent of titratable acid would be eliminated. This theory is implied in a number of text-books of biochemistry.

According to the *carbonic acid filtration theory* the glomerular ultrafiltrate not only contains phosphate but also carbonic acid and sodium bicarbonate. Sendroy, Seelig and Van Slyke[7] developed this theory on the assumption that the renal tubules are completely impermeable to carbonic acid and that they actively reabsorb sodium bicarbonate. Accordingly the reaction between dibasic phosphate and carbonic acid occurring within the tubular lumen is forced to the right by the reabsorption of bicarbonate. The monobasic phosphate which is formed is excreted in the urine as titratable acid.

According to the *tubular ionic exchange theory,* a tubular secretory mechanism is responsible for the elimination of acid in the urine, not a filtration-reabsorption mechanism as is implied in the first two theories. The significant constituents of the glomerular filtrate are considered to be monobasic and dibasic phosphate. Bicarbonate and carbonic acid are presumed to be reabsorbed in large part by the renal tubules, and therefore need not be considered. In the passage of the filtrate down the tubules, hydrogen ions derived from the tubular cells are exchanged for sodium ions in the tubular lumen. Dibasic phosphate is thereby converted to monobasic phosphate, and base is returned to the blood. The source of the hydrogen ions is presumably carbonic acid formed within the renal tubular cells. This theory was originally advanced by Homer Smith.[8]

It is significant that any one of these three theories is adequate to explain the titratable acidity and the pH of normal urine. Yet no critical experiment has appeared in the literature which either proves one theory or rules out another. Since the mechanism for acidifying the urine is a major renal homeostatic mechanism and since failure of the adequate excretion of acid in disease leads to the development of clinical acidosis, it seemed worth while to attempt to determine the nature of this mechanism.

It occurred to us that it should be possible to test these three theories experimentally, for each has inherent within it a specific identifiable limitation of its capacity to cause the excretion of acid. You will note in the *phosphate reabsorption theory* and in the *carbonic acid filtration theory* that all the acid excreted in the urine was originally present in the glomerular filtrate. In the first theory monobasic phosphate constitutes the filtered acid, and the quantity of this compound which appears in the urine as titratable acid is limited by the capacity of the renal tubules to reabsorb the dibasic phosphate which accompanies it. In the second theory carbonic acid constitutes the filtered acid, and the quantity of titratable acid excreted can not exceed the quantity of carbonic acid originally filtered. These two theoretical mechanisms are therefore limited by the measurable capacity of the tubules to reabsorb and by the measurable capacity of the glomeruli to filter. In sharp contrast the *ionic exchange mechanism* is limited by the measurable capacity of the tubules to secrete. The acid appearing in the urine is not that which was originally filtered but is that which the renal tubules have added to the filtrate by a type of secretory process, namely, ionic exchange.

We have tested these three theories in unanesthetized dogs in the following manner. The renal mecha-

[7] J. Sendroy, Jr., S. Seelig and D. D. Van Slyke, *Jour. Biol. Chem.*, 106: 479, 1934.

[8] H. W. Smith, "The Physiology of the Kidney." New York: Oxford University Press. 1937.

nism for acidifying the urine was stimulated by the repeated feeding of dilute hydrochloric acid. After the establishment of a suitable acidosis the animals were provided with a large excess of phosphate in continuous intravenous infusions. The rate of excretion of titratable acid in the urine was then compared with the rate of reabsorption of phosphate and with the rate of filtration of carbonic acid. It was found that the observed rate of excretion of acid far exceeds that which can be explained by the *phosphate* or *carbonic acid theories*. Since monobasic phosphate and carbonic acid are the only acids present in the glomerular filtrate in significant amounts, it is evident that acid must be added to the filtrate by some type of tubular secretory mechanism. We are convinced that the *ionic exchange theory* adequately describes that mechanism.

I should like to present these experiments for your critical appraisal, but let us first review briefly the methods by which we propose to solve our problem.

TABLE 3

AN EXPERIMENT ON AN ACIDOTIC DOG DESIGNED TO TEST CRITICALLY THE SEVERAL THEORIES OF THE NATURE OF THE RENAL MECHANISM FOR ACIDIFYING THE URINE

Rate of glomerular filtration cc/min.	Arterial plasma concentration			Rate of phosphate reabsorption mM./min.	Rate of H_2CO_3 filtration mM./min.	Urine pH	Rate of excretion		
	Total CO_2 mM./L.	pH	Phosphate mM./L.				Phosphate mM./min.	Creatinine mM./min.	Titratable acid mEq./min.
73.1	18.7	7.34	8.37	0.123	0.075	6.06	0.489	0.171	0.310
76.4	18.7	7.34	8.41	0.128	0.078	6.02	0.514	0.168	0.340
76.9	18.6	7.37	8.53	0.131	0.073	6.26	0.525	0.163	0.298
75.1	18.5	7.39	9.00	0.138	0.068	6.32	0.538	0.166	0.297

It is obvious that the key to the solution lies in knowing the rate at which plasma is filtered through the glomeruli, for if we know the glomerular filtration rate and simultaneously determine the concentration of carbonic acid and phosphate in the plasma, we can readily calculate the rate at which these materials are filtered through the glomeruli. Dr. Smith and his associate have given us in the creatinine clearance a ready accurate means of determining the rate of filtration of plasma through the glomeruli of the dog. In Fig. 2 we have illustrated the principles involved in a quantitation of the rate of reabsorption of phosphate. The same principles may of course be applied to carbonic acid. The rate of filtration of phosphate is obviously the product of the rate of filtration of plasma through the glomeruli, as measured by the creatinine clearance, and the concentration of phosphate in each cc of that plasma. The rate of excretion of phosphate in the urine is the product of the urine flow in cc per minute and the urine phosphate concentration. The rate of phosphate reabsorption is obviously equal to the rate of filtration minus the rate of excretion.

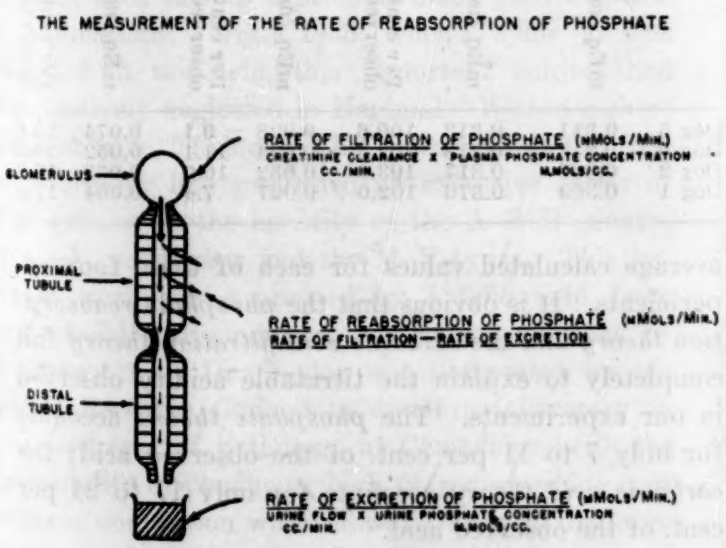
THE MEASUREMENT OF THE RATE OF REABSORPTION OF PHOSPHATE
GLOMERULUS
PROXIMAL TUBULE
DISTAL TUBULE
RATE OF FILTRATION OF PHOSPHATE (MMOLS/MIN.)
CREATININE CLEARANCE X PLASMA PHOSPHATE CONCENTRATION
CC./MIN. MMOLS/CC.
RATE OF REABSORPTION OF PHOSPHATE (MMOLS/MIN.)
RATE OF FILTRATION — RATE OF EXCRETION
RATE OF EXCRETION OF PHOSPHATE (MMOLS/MIN.)
URINE FLOW X URINE PHOSPHATE CONCENTRATION
CC./MIN. MMOLS/CC.

FIG. 2

Our experiments have been performed on trained unanesthetized female dogs, chosen for their even dispositions and ready cooperation. Urine was collected by catheter and blood samples were drawn from the femoral artery. Table 3 summarizes the significant data obtained in one experiment consisting of four identical clearance periods. It is apparent from the first column that this dog had a glomerular filtration rate slightly more than half that of an adult human. The next two columns indicate that the animal had a moderate acidosis, produced by the repeated feeding of hydrochloric acid. The normal carbon dioxide content of dog plasma, like that of the human, ranges between 23 and 26 millimols per liter, so that values of 18 to 19 millimols per liter are indicative of moderate reduction and hence of moderate acidosis. Arterial pH was determined directly by a hypodermic type glass electrode, and as you see, the observed values are slightly below the normal of pH 7.4, again indicative of moderate acidosis. The plasma phosphate concentration was elevated to some 8 to 9 times the normal by the continuous intravenous infusion of neutral sodium phosphate. The next two columns, the rate of phosphate reabsorption and rate of carbonic acid filtration, were determined by the methods we have just described. The urine pH, and in the last column, the titratable acid of the urine were

determined electrometrically, that is, the urines were titrated from their observed pH to the pH of the plasma, using the glass electrode as the measuring instrument. This titration therefore represents the reversal of the process of acidification of the urine which was performed by the kidney. The average excretion of titratable acid in this experiment is 0.311 milliequivalents per minute. In more familiar terms this is equivalent to the excretion of 4,500 cc of N/10 titratable acid per day, which is some 3 times the maximum ever observed in severe diabetic acidosis in man. The factor which accounts for this high rate of excretion of titratable acid is the very high rate of excretion of phosphate.

TABLE 4

FORMS OF THE HENDERSON-HASSELBALCH EQUATION USED IN THE ANALYSIS OF THE DATA

1. $pH = pK' + \text{Log} \frac{(\text{salt})}{(\text{acid})}$
2. $pH = 6.8 + \text{Log} \frac{(Na_2HPO_4)}{(NaH_2PO_4)}$
3. $pH = 6.1 + \text{Log} \frac{(NaHCO_3)}{(H_2CO_3)}$
4. $pH = 4.97 + \text{Log} \frac{(\text{Creatinine})}{(\text{Creatinine–HCl})}$

In order to analyze the data further we have applied the Henderson-Hasselbalch equation in the several ways which we shall describe presently. The general form of this equation is given in the top line of Table 4. Since in our experiments we must deal with three buffers—phosphate, bicarbonate, and creatinine—we must apply the equation in the three forms listed below. We have directly measured the pH and the total concentration of these three buffers in both blood and urine. From these measurements it is possible to calculate the concentration of the acidic and basic component of each buffer and the absolute contribution of the acid component of each buffer to the titratable acidity of the urine.

TABLE 5

A CRITICAL ANALYSIS OF THE DATA FROM TABLE 3 WHICH INDICATES THE INADEQUACY OF THE PHOSPHATE AND CARBONIC ACID THEORIES AND THE NECESSITY FOR POSTULATING SOME TYPE OF TUBULAR SECRETORY MECHANISM FOR ACIDIFYING THE URINE

Titratable acid of urine						
Observed	Calculated from total buffer excreted		Calculated from phosphate reabsorption theory		Calculated from carbonic acid filtration theory	
mEq./min.	mEq./min.	Per cent. of observed	mEq./min.	Per cent. of observed	mEq./min.	Per cent. of observed
0.310	0.312	100.6	0.028	9.0	0.075	24.2
0.340	0.339	99.7	0.029	8.5	0.078	22.9
0.298	0.300	100.6	0.028	9.4	0.073	24.5
0.297	0.300	101.0	0.028	9.4	0.068	22.9
0.311	0.313	100.6	0.028	9.1	0.074	23.6

In Table 5 the data of the preceding experiment have been subjected to rigorous analysis. The first column repeats the observed titratable acidity of the urine. Then applying the Henderson-Hasselbalch equation we calculated the titratable acidity in the three ways noted in the succeeding three pairs of columns. First we calculated the acidity from the measured pH of the urine and from the measured excretion rate of the several buffers. The agreement with the observed acidity is remarkable, averaging a shade over 100 per cent. This calculation is in reality a check on the accuracy of all our measurements, and it merely indicates that our data are good and deserving of further analysis. The quantity of titratable acid which could be excreted if the *phosphate reabsorption theory* were correct is rather low, averaging only 9.1 per cent. of the observed titratable acid. Similarly, the *carbonic acid filtration theory* falls short of explaining the acidity of the urine in this experiment, averaging only 23.6 per cent. of the observed titratable acid.

Four experiments in all were performed on four dogs. Each experiment was identical to that which we have just presented. Table 6 summarizes the average calculated values for each of these four experiments. It is obvious that the *phosphate reabsorption theory* and the *carbonic acid filtration theory* fail completely to explain the titratable acidity observed in our experiments. The *phosphate theory* accounts for only 7 to 11 per cent. of the observed acid; the *carbonic acid theory* accounts for only 17 to 24 per cent. of the observed acid.

TABLE 6

SUMMARY OF 4 EXPERIMENTS ON ACIDOTIC DOGS ANALYZED ACCORDING TO THE METHOD OUTLINED IN TABLE 5

Titratable acid of urine						
Observed	Calculated from total buffer excreted		Calculated from phosphate reabsorption theory		Calculated from carbonic acid filtration theory	
mEq./min.	mEq./min.	Per cent. of observed	mEq./min.	Per cent. of observed	mEq./min.	Per cent. of observed
Dog 5	0.311	0.313	100.6	0.028	9.1	0.074	23.6
Dog 6	0.213	0.218	102.3	0.024	11.1	0.052	24.5
Dog 2	0.307	0.317	103.0	0.032	10.5	0.053	17.3
Dog 1	0.369	0.376	102.0	0.027	7.4	0.064	17.2

(To be concluded)

OBITUARY

GEORGE LEES TAYLOR

THE premature death of Dr. George L. Taylor on March 9 at the age of forty-seven years is a serious loss to the field of serology that will be felt keenly, particularly by those workers interested in the branch dealing with the blood group differences and their practical applications. Dr. Taylor was born in Ashton-under-Lyne, England, on June 26, 1897. At the University of Manchester, as a medical student, he gained distinctions in anatomy, pathology and surgery (M.B. thesis) and won the Dumville surgical prize. At Manchester Royal Infirmary he was house-surgeon to Sir William Thorburn in 1919 and house physician to Dr. G. R. Murray in 1920–21; at St. Mary's Hospital in Manchester he then spent a year as obstetric house-surgeon. In 1929, after having spent a number of years in the general practice of medicine, he decided to devote himself to medical research and teaching. For six years he worked as John Lucas Walker student under Professor H. R. Dean in the department of pathology at Cambridge. From 1935 to his death he directed a unit in London particularly devoted to the study of blood groups in relation to human genetics. In 1930, he took his M.D. with commendation at Manchester, and in 1932 he obtained his Ph.D. at Cambridge. In 1939 he was elected a member and, in 1944, a fellow to the Royal College of Physicians.

Taylor's scientific contributions fall into two principal categories. His earlier investigations, carried out from 1929 to 1935 in close association with Dean and the two Adairs, dealt chiefly with the precipitin reaction. His findings are described in a series of ten papers which illustrate well Taylor's thoroughness and pertinacity in carrying out investigative work. Taylor's subsequent publications, comprising some 30 papers in which he was author or collaborator, dealt with various aspects of blood grouping and its applications. Until 1935, when Taylor became interested in the field, this important subject had been relatively neglected in England. Within a short period of time, Taylor and his coworkers at the Galton laboratory had published an extensive series of investigations on the heredity of the A–B–O groups, the A_1–A_2 subgroups and the M–N types. This important work was supported by a fellowship from the Rockefeller Foundation, and at the outbreak of the present war, Dr. Taylor was designated by the Medical Research Council to direct a laboratory in the department of pathology at Cambridge, with the responsibility of producing high-titered grouping sera for use in connection with the war. Despite the large amount of routine work this task entailed, the unit under Dr. Taylor's direction achieved a remarkable amount of excellent research work, particularly in the complex field of the Rh blood factors and their applications. The beginning of the Rh work in England can be dated from a letter which appeared in the *British Medical Journal* on May 2, 1942, in which Taylor and Mollison appealed to physicians for specimens of blood from mothers of infants with erythroblastosis fetalis. Within a year Taylor became known to hundreds of practitioners throughout the United Kingdom, and spared no pains to explain to physicians and patients the significance of this new blood factor. Within twenty months the Cambridge unit had discovered seven alleles in the Rh series of genes, their report appearing only a month or two following the report by Wiener of six allelic Rh genes, thus independently corroborating and extending Wiener's work. A particularly generous gesture by Taylor was that he did not hesitate to adopt Wiener's nomenclature for the Rh genes, though their existence had been separately discovered by Taylor and his colleagues.

It is fitting to close with the following quotation of a statement by one who knew Dr. Taylor intimately as a man as well as a scientist. "You had to know him well to realize that whatever cares he had were primarily cares for the welfare of others; and that the determination of his character was sustained by a warmth of feeling which sought, in general practice as well as in research, to alleviate the suffering of his fellows. If the motive of medicine is service and not personal gain, George Taylor was a good doctor."

A. S. WIENER

RECENT DEATHS

DR. GEORGE B. RAY, executive director of the department of physiology and pharmacology of the Long Island College of Medicine, died on July 6. He was fifty-two years old.

DR. JOHN L. HOGG, from 1920 to 1936 research engineer of the Bell Telephone Laboratories, previously professor of physics at McMaster University, Toronto, died on July 4 at the age of seventy-four years.

LAWRENCE JOHN PALMER, from 1937 to 1944 principal biologist in the investigations of the Wildlife Resources of Alaska for the Fish and Wild Life Service of the Department of the Interior, died on June 20 at the age of fifty-two years.

DR. EDWARD BARCLAY-SMITH, the British anatomist, died on July 5 at the age of eighty-four years. He was formerly dean of the faculty of medicine at King's College, University of London.

MEMORIAL services for Dr. Harold Hibbert, professor of industrial and cellulose chemistry at McGill University, who died on May 13 at the age of sixty-seven years, were held at Pawling, N. Y., on July 8.

SCIENTIFIC EVENTS

THE OFFICE OF WAR INFORMATION

ELMER DAVIS, director of the Office of War Information, and Neil Dalton, director of the Domestic Branch of the Office, have made the following announcement:

The facilities of the Office of War Information, Domestic Branch, have been made available to the newly organized Joint Board on Scientific Information Policy for the handling of information on scientific and technical developments of the Government during the war.

The Joint Board on Scientific Information Policy will be responsible for the organization and release of scientific and allied information for the Office of Scientific Research and Development, the War and Navy Departments and the National Advisory Committee for Aeronautics.

The chairman of the board is Dr. John T. Tate, division chief, National Defense Research Committee, Office of Scientific Research and Development. Other members are: Rear Admiral Harold G. Bowen, U.S.N., chief, Office of Research and Inventions, Department of the Navy; Colonel Douglas Parmentier, U.S.A., chief, News Division, Bureau of Public Relations, War Department; Captain Waldo Drake, U.S.N.R., deputy director, Office of War Information, and Dr. George W. Lewis, director of aeronautical research, National Advisory Committee for Aeronautics. John Tait Milliken, chief of the Weekly Press Division, Office of War Information, is executive secretary.

The Joint Board on Scientific Information Policy has been created by concurrent action on the part of the Secretary of War, the Secretary of the Navy and Dr. Vannevar Bush, director of the Office of Scientific Research and Development, with the consent of the chairman of the National Advisory Committee for Aeronautics and the director of the Office of War Information. Its creation was in accordance with the recommendation of the Joint Committee on Scientific Information Policy, consisting of the Secretaries of War and Navy and the director of the Office of Scientific Research and Development, to study the problem of supplying the general public with authentic and useful information on wartime scientific developments.

The committee said in its report "that a positive information policy is desirable to supplement spot news stories, which probably can never be controlled as to accuracy of content or interpretation of scientific development; that the basic purpose of such a policy is to establish in the minds of the public a proper concept of how scientific development really has taken place; . . . and that the work of carrying out such a policy should be entrusted to a small group of personnel whose duties shall include determining suitable stories, getting the necessary background of information from the laboratories and operational units concerned, and in general guiding the story to a release point. . . ."

The basic reports of the board will include such fundamental subjects of moment as radar rockets, metallurgy, jet propulsion, aircraft design, and public health, medicine, plastics, etc.

In addition to clearing and issuing basic releases on scientific developments, the board, through its office at the Office of War Information, Domestic Branch, Social Security Building, Washington, D. C., will carry out its directive function of assisting writers and publications through appropriate contacts, clearances and working information. Consideration will be given by the board to the special request of all branches of publishing, professional writers, radio and motion pictures. The existing facilities of the Domestic Branch of the Office of War Information will be provided for this purpose.

THE AMERICAN CONGRESS ON SURVEYING AND MAPPING

THE American Congress on Surveying and Mapping held its fifth annual meeting in Washington, D. C., on June 23. Commander Frank S. Borden, of the U. S. Coast and Geodetic Survey, was elected president; Major Richard T. Evans was named secretary-treasurer, and A. L. Shalowitz was named editor of *Surveying and Mapping*, the quarterly journal of the congress. The meeting included a panel discussion on "Cooperation among the Technical Organizations," in which representatives from the American Society of Civil Engineers, the American Society of Photogrammetry, the American Geophysical Union and the American Congress on Surveying and Mapping participated.

The Congress on Surveying and Mapping was organized in 1941 for the purpose of advancing the sciences of surveying and mapping and to contribute to public education in the use of maps and to encourage the promotion of basic mapping programs.

THE AMERICAN STANDARDS ASSOCIATION

CHANGES in the constitution of the American Standards Association that will enable it to meet more fully the needs of government and industry in the postwar period have been announced by P. G. Agnew, secretary of the association. The national trade, technical and governmental groups that make up the association have ratified these changes, the principal one of which will remove present restrictions limiting the

work of the association "to those fields in which engineering methods apply" so that the organization can in the future handle any standard or standardization project which is in the field of engineering or consumer goods or in any other field which deserves national recognition.

Another change provides for specific mention of the consensus principle in the constitution. This principle—that all groups with an interest in a particular standard have a right to a voice in its development—has always been basic in the association operations. It seemed wise to place additional emphasis upon it by incorporating it in the constitution, thus assuring cooperating bodies that the work will be carried out in accordance with their desires.

A third change provides for election to the board of directors of three members-at-large. At present all but the members of the board are nominated in rotation by the member-bodies. The additional members-at-large will make it possible to enlist the services of outstanding persons from groups not otherwise represented, thus making the board still more broadly representative.

In making these changes in the constitution of the American Standards Association, the national trade, technical and governmental groups that constitute its basic membership restated their belief that the central force of the standardization movement should continue to spring from the organized industrial, professional and consumer groups with the full cooperation of the governmental agencies concerned.

THE BRITISH GUIANA NATURAL HISTORY MUSEUM

THE British Guiana Natural History Museum, including laboratory, library, collections, vivarium and aquaria, as well as their expertly mounted and exhibited specimens and habitat groups, was destroyed this spring by a fire originating in an adjacent store. Plans are being made to re-establish this museum, and to make a major expedition into the hinterland of British Guiana (Mount Roraima area) for the replacement of specimens of the flora and fauna. It is hoped to start this expedition in the fall of this year.

The museum is desirous of getting into communication with any party that might be interested in joining the expedition, on the basis of a 50–50 split of all specimens collected. It is also interested in corresponding with any institution prepared to exchange natural history specimens.

The museum is also interested in receiving catalogues of taxidermy supplies and miscellaneous museum equipment—glass for large cases, glass jars, aquaria, collecting apparatus, etc.; and reference books, particularly relating to taxidermy.

Any one having information relative to the reconstruction of a small first-class museum can address R. S. Singh, preparator, British Guiana Natural History Museum, Georgetown, B. G.

NEWS OF EUROPEAN INVESTIGATORS

DR. FRANZ SCHRADER, of Columbia University, writes that he has heard from Dr. Jean Le Calvez, formerly vice-director of the Marine Laboratory at Banyuls sur Mer. "Le Calvez was taken prisoner by the Germans in 1940, but in 1942 was permitted to go to the Kaiser Wilhelm Institut für Biologie, where he carried on his research in Dr. H. Bauer's department. The institut was shifted to Hechingen in Württemburg in 1943 and was not damaged when the French troops took over the town in April, 1945." Dr. Le Calvez's personal news will, I think, be of interest to many American biologists: "Professor H. Bauer and Dr. J. Straub were both well when the French occupied Hechingen; Professor M. Hartmann was at that time staying on his country place in southern Germany; Dr. K. Pätau had remained in Berlin-Dahlem when the institut was shifted, and there had been no recent news of him; Dr. Schartau was killed in an airplane accident; Professor F. von Wettstein died of a pulmonary infection early in 1945; Professor N. W. Timofeeff-Ressovsky was still in Berlin-Buch in March, 1945, but nothing had been heard of him since that time."

Dr. Wm. Randolph Taylor, of the University of Michigan, writes as follows: "Dr. F. Børgesen writes that he is continuing his researches on Mauritius algae at the Botanical Institute, Copenhagen, and has been able to publish some work during the war. Dr. Børgesen is best known for his very important work on the marine algae of the Danish West Indies, but has also made major contributions to our knowledge of the algae of Easter Island, the Faröes Islands, the Canary Islands and India.

"Mme. P. Lemoine, formerly at the Museum National d'Histoire Naturelle, Paris, writes from La Bezole, Villelongue, Aude, that she spent the period of the war without acute suffering. Mme. Lemoine is a well-known student of coralline algae, especially the massive reef-inhabiting types, and has monographed them for several notable expeditions, for Dr. F. Børgesen's studies on Danish West Indian algae and other important works."

Dr. Curt Stern, of the University of Rochester, writes: "I have some information about European scientists which may be of interest to the readers of SCIENCE. I learned from a letter from Dr. F. Baltzer, professor of zoology at the University of Bern, Switzerland, that Dr. von Frisch, professor of zoology at the University of Munich, is alive. The laboratory in Munich has been destroyed. Also I have received reprints from Professor Dontcho Kostoff, of the Uni-

versity of Sofia, Bulgaria, showing that Professor Kostoff has been active scientifically all through the war and is still working in Sofia."

ANNIVERSARY OF THE ACADEMY OF SCIENCES OF THE SOVIET UNION

THE names of American scientific men who left New York early in June to attend at the invitation of the Soviet Government the two hundred and twentieth anniversary of the Academy of Sciences of the Union of Soviet Socialist Republics, which was held from June 15 to 28 in Moscow and Leningrad, were given in the issue of SCIENCE for June 15. A party of scientific men left England for Russia on June 13. A farewell party was held at Burlington House, London, on the preceding day, when the scientists met the Soviet Ambassador, Mr. Gusev, and members of the Royal Society. It was arranged that members of the party would include:

Professor N. K. Adam, F.R.S., Professor E. N. da C. Andrade, F.R.S. (representing the Physical Society; also the University of London), Professor E. D. Adrian, F.R.S. (also representing the University of Cambridge), Professor J. D. Bernal, F.R.S., Professor P. M. S. Blackett, F.R.S., Professor Max Born, F.R.S., Professor V. Gordon Childe, F.S.A. (also representing the Royal Society of Edinburgh), Dr. E. M. Crowther, F.I.C., Sir Charles Darwin, F.R.S. (also representing the Institution of Naval Architects), Professor P. A. M. Dirac, F.R.S., Professor F. G. Donnan, F.R.S. (also representing the Chemical Society), Mr. W. N. Edwards, F.G.S., Professor C. N. Hinshelwood, F.R.S. (also representing the University of Oxford), Sir Thomas Holland, F.R.S. (representing the Geological Society), Dr. J. S. Huxley, F.R.S., Sir Harold Spencer Jones, F.R.S. (Astronomer Royal), Professor E. A. Milne, F.R.S., Professor N. F. Mott, F.R.S., Dr. Alex Muir, Professor R. G. W. Norrish, F.R.S., Dr. W. G. Ogg, Lord Radnor (representing the Rothamsted Experimental Station), Professor E. K. Rideal, F.R.S., Sir Robert Robinson (representing the Royal Society of London), Professor A. Sorsby (representing the Anglo-Soviet Medical Council), Professor R. H. Tawney, Dr. Henry Thomas, F.B.A., F.S.A. (representing the British Museum), Professor D. M. S. Watson, F.R.S. (also representing the British Association), and Dr. W. A. Wooster (representing the Association of Scientific Workers).

At the last minute, however, the Government refused to allow eight of the group to leave the country because the work on which they were engaged was too important to put aside.

The men who were not allowed to go were Sir Charles Darwin, Professor Blackett, Professor Norrish, Professor Bernal, Professor Dirac, Professor Mott, Professor Milne and Professor Rideal. All are engaged on work of the greatest importance in the production of war materials and research.

SCIENTIFIC NOTES AND NEWS

THE honorary doctorate of laws was conferred on June 23 by the University of California on Dr. Lewis M. Terman. On June 28, at Harvard University, his son, Dr. Frederick E. Terman, director of the radio research laboratory, was awarded the honorary doctorate of science.

THE University of Hawaii conferred the degree of doctor of laws on Thomas A. Jaggar at its thirty-fourth annual commencement exercises on June 12. Dr. Jaggar gave the commencement address, which was entitled "The Great Reversal."

THE honorary degree of doctor of science has been conferred by the University of Manitoba on Dr. Thorbergur Thorvaldson, head of the department of chemistry of the University of Saskatchewan.

DR. WARD V. EVANS, chairman of the department of chemistry of Northwestern University, will receive the 1945 Honorary Scroll Award from the Chicago Chapter of the American Institute of Chemists, in recognition of his "outstanding achievements in the field of chemistry, as a great teacher, as an industrial consultant, and for his high civic spirit." He will retire on September 1, after having been a member of the faculty of the university since 1916. Past recipients of the Honorary Scroll Award have included Professor V. N. Ipatieff, of Northwestern University; Dr. F. C. Koch, of the University of Chicago, and Dr. R. B. Harper, of the Peoples Gas Light and Coke Co.

IT is reported in the *British Medical Journal* that during his recent tour in Sweden to lecture on penicillin, under the auspices of the British Council and at the invitation of the Swedish Medical Society, Sir Howard Florey, F.R.S., was honored with the presentation of the Berzelius Medal in Silver. This medal was presented to members of the Swedish royal family and certain other distinguished persons when it was instituted in 1850. It has not been awarded since that time.

THE Legion of Merit has been awarded to Lieutenant Colonel Arthur H. Warner, associate professor of physics at the University of California at Los Angeles and head of the technical section of the air defense division of the Supreme Headquarters of the Allied Expeditionary Forces, "for his excellent work during the European invasion and campaign."

He is expected to remain in Europe for some time to carry on scientific work for the Army.

COLONEL JUSTIN M. ANDREWS, Sn.C., chief malariologist for the Mediterranean Theater of Operations, has returned to the United States from service overseas in Africa and Italy. He has been awarded the Legion of Merit in recognition of his outstanding accomplishments in directing malaria control activities of the U. S. Army.

THE list of birthday honors of the King of England includes the name of Dr. C. E. Inglis, lately professor of the mechanical sciences at the University of Cambridge, who has been designated Knight Bachelor.

THE first meeting of the new Society for the Study of Blood was held at the New York Academy of Medicine on June 14. The following addresses were delivered: Dr. Nathan Rosenthal, "The Development of Hematology in New York City"; Dr. Eugene R. Marzullo, "The Role of the Hematologist in the General Hospital"; Dr. Lester J. Unger, "Blood Banks of the Future." The society will concern itself with the allied fields of hematology, blood grouping and blood transfusion, and scientific meetings are to be held three times a year. The officers elected for the first year are: *President,* Dr. Alexander S. Wiener; *Vice-president,* Dr. Paul Reznikoff; *Secretary-Treasurer,* Dr. Peter Vogel.

SIR PEIRSON FRANK, chief engineer of the London County Council, has been elected president of the British Institution of Civil Engineers.

E. G. BAILEY, a vice-president of the Babcock and Wilcox Company, manufacturers of steam generating equipment, has been elected an honorary member of the British Institution of Mechanical Engineers.

DR. IVAN C. HALL has resigned as professor of bacteriology and director of the department of bacteriology of the New York College of Medicine.

DR. CHARLES RUSSELL BURROWS, since 1925 professor of electrical engineering of the Bell Telephone Laboratories, has been appointed director of the School of Electrical Engineering of Cornell University. He succeeds Professor W. A. Lewis, who resigned recently.

LAUREN EARL SEELEY, associate professor of mechanical engineering at Yale University, has been appointed dean of the College of Technology of the University of New Hampshire. He will succeed George W. Case, whose retirement was announced recently. Leon W. Hitchcock, professor of electrical engineering, has been serving as acting dean of the college, and will continue to serve in that capacity until the arrival of Mr. Seeley.

DR. JAMES BERNARD MCNAUGHT, associate professor of pathology in the School of Medicine of Stanford University, has been appointed professor of pathology at the School of Medicine at Denver of the University of Colorado.

DR. LEONARD B. CLARK has been appointed chairman of the department of biology of Union College. He succeeds Dr. James W. Mavor, since 1916 chairman of the department, who becomes research professor of biology.

DR. WILLIAM EUSTIS BROWN, formerly professor of preventive medicine at the College of Medicine of the University of Cincinnati, has been appointed dean of the College of Medicine of the University of Vermont.

PROFESSOR ALBERT E. MEDER, JR., of the department of mathematics of Rutgers University, has become dean of administration. This is in addition to his position as secretary of the university.

DR. CLIFFORD O. JENSEN, who has been associated with the P. Lorillard Company, has been appointed professor of phytochemistry, in charge of tobacco research, in the department of agricultural biochemistry of Pennsylvania State College.

DR. JOHN T. LONSDALE, professor of geology and head of the department at Iowa State College, has resigned to become director of the Bureau of Economic Geology of the University of Texas.

PROFESSOR GEORGE E. GOODMAN, of the department of botany of Iowa State College, has been appointed a professor of botany at the University of Oklahoma.

DR. CHARLES FREMONT MCKHANN, assistant in charge of research to the president at Parke, Davis and Company, of Detroit, has been named professor of pediatrics at the School of Medicine of Western Reserve University and director of pediatrics at University Hospitals, Cleveland. He succeeds Dr. Henry J. Gerstenberger, who becomes professor emeritus, as professor of pediatrics at Western Reserve and director of the Babies and Childrens and Rainbow Hospitals. Dr. John A. Toomey will remain the acting director of pediatrics at the University Hospitals until September 1. He will continue at Western Reserve University as professor of clinical pediatrics and contagious diseases, and in charge of the departments of contagious diseases at University and City Hospitals.

DR. J. T. EMLEN, JR., has been appointed research associate in the department of parasitology of the

Johns Hopkins School of Hygiene and Public Health, to take charge of investigations on rodent ecology and control. This program, which is supported by a grant from the Rockefeller Foundation, is being carried out with the cooperation of the Rodent Control Division of the City of Baltimore. It is a continuation and expansion of the field studies which Dr. Curt Richter, of the Johns Hopkins Medical School, developed during the last three years in cooperation with this division. Dr. Richter will serve on the advisory committee for this expanded program, and is continuing as part of the new program his laboratory investigations on the behavior of wild rats.

IN a recent issue of SCIENCE it was stated that Major F. W. Shotten had been appointed Sorby professor of zoology at the University of Sheffield. This should have read Sorby professor of geology.

DR. G. J. BOUYOUCOS, research professor of soils at Michigan State College, has been appointed to serve as agricultural consultant to the Government of Greece.

DR. W. G. BYWATER, for the last ten years a leader of research work on the staff of Parke, Davis and Company, has been appointed director of research of S. B. Penick and Company.

DR. ROBERT C. STEBBINS has joined the staff of the Museum of Vertebrate Zoology of the University of California at Berkeley as assistant curator in herpetology and instructor in zoology. He will be in charge of the herpetological collections.

DR. E. C. FAUST, acting head of the department of tropical medicine of Tulane University, at the request of the Surgeon General of the U. S. Army is serving as the head of a special mission to study tropical maladies in the Southwest Pacific.

PROFESSOR R. S. MARSH, head of the department of horticulture of the College of Agriculture, Forestry and Home Economics of West Virginia University, has a leave of absence for a year to enable him to organize the Department of Horticulture of the Army University Study Center at Fontainebleau, France. He sailed on July 5 on the *Queen Elizabeth*.

DR. WILLARD H. WRIGHT, chief of the zoological laboratory of the National Institute of Health, at the request of the Surgeon General of the Army, has been assigned for temporary duty and detailed for overseas service as member of a special commission to study schistosomiasis in the Southwest Pacific Area.

IT is reported in the issue of *The Times*, London, for June 27 that Professor A. V. Hill, senior secretary of the Royal Society, left England on June 26 for Copenhagen to convey the greetings of the society, as representing the men of science of Great Britain, to their colleagues in Denmark and through the Academy of Sciences in that country to discuss with them what aid British science can give to the rehabilitation of science and scientific education in their country. After three days in Copenhagen Professor Hill proceeded to Oslo for the same purpose. An extraordinary meeting of the Norwegian Academy of Sciences was called to meet him.

SIR ALEXANDER FLEMING, F.R.S., professor of bacteriology at St. Mary's Medical School, University of London, gave on July 11 a lecture on "The Development of Penicillin" before the Yale Medical Society.

THE correspondent at Moscow of *The Times*, London, writes under date of June 15: "The Soviet academicians welcomed their foreign guests, a distinguished list of nearly 200, at a reception held in a mansion on Sparrow Hills which had been the headquarters of the Academy of Sciences of the U.S.S.R. since it was transferred from Leningrad in 1934. In the afternoon it was the turn of the representatives of the exact sciences; to-night men distinguished in all fields of humane science are to assemble. To-morrow has been set aside for a plenary session to mark the 220th anniversary of the foundation by Peter the Great of the academy, which has grown into a vast organization controlling 150 scientific institutions where both pure and industrial research is carried out. During the past few days Russian aeroplanes have been bringing in learned men from all over the world—from India, China, Britain, Canada, the United States, central Europe and the Balkans. Professor Komarov, the eminent botanist, who is president of the Academy of Sciences, will preside to-night over the meeting of presidents of the many national academies assembled in Moscow."

THE California Institute of Technology has authorized the establishment of post-doctorate Gosney Research Fellowships in Biology in memory of the late E. S. Gosney. The first appointments will be for fundamental research in heredity or related subjects at the institute, and will have no teaching duties. Appointments may be made for one or two years, and reappointments may be made when desirable. It is possible that in certain cases candidates not now available will be appointed, their tenure to begin upon release from the armed forces or from war projects. The appointments will be recommended by a committee, the chairman of which is Professor A. H. Sturtevant, the California Institute of Technology, Pasadena 4, Calif.

A SCHOLARSHIP plan for the encouragement of promising young scientific students has been adopted by the Radio Corporation of America. The plan provides for ten students to receive RCA scholarships during the academic year 1945–1946, thirty during 1946–1947, fifty during 1947–1948 and sixty each academic year thereafter. Each scholarship consists of a cash award of $600. Those eligible will include all students enrolled at universities to be selected by the RCA Education Committee. Selection of students will be made upon recommendation of the dean of the specified university and approval by the committee. The chairman of the Education Committee is Dr. James Rowland Angell, president emeritus of Yale University and public service counselor of the National Broadcasting Company.

A NEW list of all American Standards and War Standards approved to date has been published by the American Standards Association and is available free of charge. There are approximately eight hundred standards listed in the booklet, covering specifications for materials, methods of tests, dimensions, definitions of technical terms, procedures, etc., in the electrical, mechanical, building, transportation, textile and other fields. For ready reference, the standards are listed alphabetically as well as by engineering fields. There is also a separate list of war standards.

THE Beit Trustees have established a Beit research fellowship to be attached to the Rhodes Livingstone Institute for Social Anthropological Research in Southern Rhodesia. The value of the fellowship is £1,250 a year for four years.

IT is reported in *Nature* that the London, Midland and Scottish Railway has announced a scheme whereby it will send members of its research staff for varying periods to carry out fundamental research in their particular fields in university laboratories; and, in exchange, the universities will be invited to send members of their staffs to spend a period in the company's research laboratory at Derby, working on applied problems in which they are interested from the fundamental side. The laboratory has a staff of seventy research workers, and has sections dealing with engineering, metallurgy, chemistry, physics, paint and textiles.

THE Czechoslovak universities were closed by the German occupational authorities as early as November, 1939, and the libraries were depleted of many valuable volumes. In addition to this calamity, Czechoslovak scientists and research workers were deprived of the benefits of being informed about the American progress in science because they were cut off from American books and journals for a period of more than six years. There is a deep interest in Czechoslovakia in reprints of articles on antibiotics, enterobacteriaceae, sulfa drugs, the Rh factor, disinfectants, control of milk and water, Rickettsial diseases, chick embryo technique, fluorometric tests, vitamins, plant diseases, animal husbandry and poultry raising, food preservation, canning, etc. It would be very much appreciated if authors of any such articles would be kind enough to send some of their spare reprints to American Friends of Czechoslovak Institutions of Higher Learning, who would forward the collected copies to proper places as soon as shipping space becomes available. These should be addressed to L. Stolfa, M.D., President, Czechoslovak Institutions of Higher Learning, 2401 Gunderson Ave., Berwyn, Ill.

IT is reported in *The Times*, London, that "a fourfold indictment of German professors and scientists who condoned and even took part in the Nazi prostitution of learning was approved unanimously at New College, University of Oxford, on July 1, by the annual conference of the International Association of University Professors and Lecturers. The resolution condemned those who 'both before and during the war furthered the Nazi régime by propounding and spreading false biological theories and so making themselves morally responsible for racial persecution. Contributed, actively or passively, to the prostitution of science for the purposes of total warfare. Were active in the destruction of university libraries, scientific laboratories and museums in the German-occupied countries. Made use of modern developments in science, particularly medicine and physiology, in order to perform, on prisoners and civilians in concentration camps, experiments resulting in mutilation or death.'"

SPECIAL ARTICLES

TROMBICULA FLETCHERI WOMERSLEY AND HEASLIP 1943, A VECTOR OF TSUTSUGAMUSHI DISEASE (SCRUB TYPHUS) IN NEW GUINEA[1]

VERY early in the war with Japan, the occurrence of tsutsugamushi disease (scrub typhus, mite fever) became a matter of military importance to troops in

[1] From the United States of America Typhus Commission, War Department and the Board for the Investigation and Control of Influenza and other Epidemic Diseases in the Army, Preventive Medicine Service, Office of The Surgeon General, U. S. Army, Washington, D. C.

New Guinea. As a result of a request from the Commanding General, Southwest Pacific Area, to the Surgeon General of the Army, a commission was formed under the auspices of the United States of America Typhus Commission and the Board for the Investigation and Control of Influenza and other Epidemic Diseases in the Army to investigate the disease in this area. A complete account of these investigations is in process of publication.[2] A brief report is herewith presented of the findings with regard to a species of mite apparently responsible for the transmission of the causative agent, *Rickettsia orientalis,* in New Guinea.

The work of Japanese investigators from 1899 to 1931 established *Trombicula akamushi* (Brumpt) 1910 as the principal, if not only, vector of the disease on Honshu, Formosa and the Pescadores Islands. A closely related species, *T. deliensis* Walch 1923, has been found to be the most common trombiculid mite parasitic in the larval stage upon wild rodents and attacking man in the endemic foci of Sumatra,[3,4,5] the Federated Malay States,[6,7,8] India[9] and North Queensland.[10,11] Up to the present time investigators have failed to bring experimental proof of its role as a vector by recovering *R. orientalis* from susceptible animals which had been injected with emulsions of "ground-up" mites or from animals on which mites had been allowed to feed, although a highly suggestive result was obtained in one experiment with a gibbon.[5]

In New Guinea, observations on mites in relation to "endemic typhus" were begun by Gunther[12] before the war. The evidence at his disposal led him to suspect *T. buloloensis* Gunther 1939 as the most likely vector, but he had been unable to test this conclusion, at the time of his report, by injection of an emulsion of suspected mites into white mice. A mite which Gunther, in 1940, classified under the name *T. vanderghinstei* (subsequently identified as *T. deliensis* by Womersley and Heaslip), obtained from rats at Bulolo, New Guinea, was dismissed from consideration because of limited distribution.

The investigations of the commission were made in an area on the northeast coast of New Guinea which is triangular in shape and delimited roughly by lines connecting Oro Bay and Buna with a native village called Inonda, which is on the Samboga River approximately 20 miles inland. This locality, known as the Dobadura area, was one of the advanced bases of supply for the military operations conducted during 1943 and 1944. A clinical and epidemiological investigation of the occurrence of scrub typhus or tsutsugamushi disease among the Army units moving into and through this base was made during the fall of 1943.

In attempting to identify the species of mite responsible for transmission in this area, larval forms[13] were collected not only from localities where cases were known to have originated and where as a result of use of the camp site extensive environmental changes had taken place, but also in similar places nearby, where natural conditions had remained undisturbed.

According to the method of collection, the larvae were divided into three groups:

(1) Those found attached to the skin of individuals who had been exposed in the field;

(2) Those which were attracted to and climbed upon the boots of the observer standing in an infested spot—"boot-collections";

(3) Those which were found attached to the skin of small animals captured in the endemic area.

Collections of mites which had become attached to the skin of individuals were few in number. Exposure of volunteers for the purpose appeared to be injudicious in view of the risk of infection with scrub typhus. The species identified from this source of material were *Schöngastia blestowei* Gunther 1939, *S. pusilla* Womersley 1944 and *T. buloloensis* Gunther 1939.

"Boot collections" were made in a large number of localities associated with the occurrence of cases of tsutsugamushi disease. The same three species mentioned above were found most frequently, and a

[2] F. G. Blake, K. F. Maxcy, J. F. Sadusk, Jr., G. M. Kohls and E. J. Bell, *Am. Jour. Hygiene,* in press.
[3] E. W. Walch, *Kitasato Arch. Exp. Med.,* 5: 63, 1923.
[4] *Idem, Kitasato Arch. Exp. Med.,* 6: 235, 1925.
[5] E. W. Walch and N. C. Keukenschrijver, *Archiv für Schiffs- und Tropen-Hygiene Pathologie und Therapie Exotischer Krankheiten,* Beiheft 1, 29: 420, 1925.
[6] B. A. R. Gater, Trans. of the Eighth Congress, Far Eastern Assoc. of Trop. Med., Siam, 2: 132, 1930.
[7] *Idem, Parasitol.,* 24: 143, 1932.
[8] R.Lewthwaite and S. R. Savoor, *Lancet,* 1: 255 (Part I), 1940; *Lancet,* 1: 305 (Part II), 1940.
[9] D. R. Mehta, *Ind. Jour. Med. Research,* 25: 353, 1937.
[10] W. G. Heaslip, *Med. Jour. Australia,* 2: 555, 1940.
[11] *Idem, Med. Jour. Australia,* 1: 380, 1941.
[12] Carl E. M. Gunther, Proc. Sixth Pacific Science Congress of the Pacific Science Asn., 5: 715, 1942.

[13] Specimens were identified quite largely on the basis of the papers "The Trombiculinae (Acarina) or Itch-mites of the Austro-Malayan and Oriental Regions," by H. Womersley and W. G. Heaslip (*Trans. Royal Soc. S. Australia,* 67: 68, 1943), and "Notes on and Additions to the Trombiculinae and Leeuwenhoekiinae (Acarina) of Australia and New Guinea," by H. Womersley (*Trans. Royal Soc. S. Australia,* 68: 82, 1944). In these two papers 33 species are recorded for New Guinea, a few of which may be regarded as of tentative rather than of established validity and are still under consideration by Womersley and others. This applies to the species *Trombicula fletcheri* and *Trombicula walchi,* to which reference will be made later. We are indebted to Mr. Womersley, South Australian Museum, Adelaide, for checking identifications of representative specimens collected in our investigation.

fourth, *T. kohlsi* Womersley 1944, was common. Two species less commonly found are particularly important, namely, *T. fletcheri* Womersley and Heaslip 1943 and *T. walchi* Womersley and Heaslip 1943. Four species were rarely found in boot collections: *T. scincoides,* Womersley 1944, *Guntherana bipygalis* (Gunther) 1939, *Guntherana parana,* Womersley 1944 and *Leeuwenhoekia nova-guinea,* Womersley 1944.

From boot collections and from the previous observations of McCulloch[14] it was apparent that *S. blestowei, S. pusilla* and *T. buloloensis* were abundant and widely distributed. These three species appeared to be principally responsible for the "scrub itch" from which troops suffered in certain areas, but it seemed unlikely that they served as vectors of *Rickettsia orientalis.* They continued to be present in considerable numbers in infected localities after the incidence of tsutsugamushi disease had become sporadic or ceased altogether. There was no correlation between the occurrence of "scrub itch" and that of tsutsugamushi disease. Patients with this disease gave no history of itching at the site of the primary lesion or eschar produced by the infective feeding. These lesions or eschars were found on various parts of the body, while the lesions of "scrub itch" were characteristically distributed on the ankles, legs and, to a lesser extent, over the lower trunk.

The survey of the mites infesting local host animals in the Dobadura area of New Guinea involved the examination of 55 rats,[15] 28 bandicoots (*Echymipera cockerelli*), 1 wallaby, 2 birds and 3 lizards. On small animal hosts larvae were found attached singly at various sites or in closely packed orange-red or whitish colonies numbering up to 300 or more individuals in each. Colonies were composed of one or more species and were usually situated in the conchae of the ears, on the ear margins and in the region of the genitalia.

In view of the previous work with tsutsugamushi disease, attention was concentrated upon rats and a marsupial, the bandicoot, since the possibility existed that the reservoir host of *R. orientalis* would be found among these animals. No rodents other than rats were found in the area concerned. Interest in mites was centered upon larvae of the genus *Trombicula,* although 5 other genera were represented in the collections from animal hosts. Table 1 summarizes the identifications of mites of this genus from rats and bandicoots.

[14] R. N. McCulloch, *Med. Jour. Australia,* 2: 543, 1944.

[15] Species determinations were made through the courtesy of Mr. E. L. Troughton, of the Australian Museum, Sydney, as follows: 29 *Rattus concolor browni,* 7 *R. mordax,* 3 *R. praetor* (?), 5 *R. gestri* (?), 7 *Melomys* sp., 1 *Uromys lamington,* 3 rats, sp. undetermined.

TABLE 1

Mite species	Found on rats		Found on bandicoots	
	Number of animals	Number of specimens	Number of animals	Number of specimens
Trombicula fletcheri	25	250	22	399
Trombicula deliensis	3	40	0	0
Trombicula walchi	4	5	5	28
Trombicula buloloensis	2	2	3	4

T. fletcheri, a species closely allied to *T. akamushi,* was by far the most prevalent and abundant species on both rats and bandicoots. Since it had been encountered in boot-collections it presumably also attacked man. Next in importance on these hosts was *T. deliensis* and the closely related if not identical species, *T. walchi,* which had also been taken in boot-collections. *T. buloloensis* was least frequently taken. Few *S. blestowei* and no *S. pusilla* were found on these hosts.

In an effort to recover *R. orientalis,* eight pools of larval mites (7 from bandicoots and 1 from a rat, *R. mordax*) were emulsified and injected intraperitoneally into groups of 4 mice, each group receiving the emulsion from a single animal. Part of each pool was retained for species identification. The results with six of these pools were negative; two were positive. Both were from bandicoots.

From one (Host 21) over 300 larval mites were removed. Approximately 100 were retained for identification and the rest used for the inoculation. All the 69 specimens which were examined were classified as *Trombicula fletcheri.* From the other bandicoot (Host 22), similarly infested, about 90 mites were retained for identification and the rest, about 150 or more, were injected into mice. In the sample lot which was examined there were 63 *T. fletcheri,* 1 *T. walchi* and 1 *Guntherana parana.*

The rickettsial strains which originated from these two mite pools were designated *No. 21 mite strain and No. 22 mite strain.* These strains were continued by passage in mice and compared with strains recovered by inoculations of mice with blood from patients suffering from tsutsugamushi disease infected in the same area. Immunity tests between the strains of mite origin and a strain of human origin carried out in rabbits, hamsters and Swiss mice indicated complete cross protection. The human and mite strains were identical in behavior and exhibited the characteristics of *R. orientalis.*

Brain tissue from both bandicoots (Hosts 21 and 22), injected into mice, failed to produce rickettsial infection. Up to the present there is no convincing evidence that the bandicoot is a reservoir host. Since *R. orientalis* may be passed in mites from one gen-

eration to the next, it does not follow that the positive pools were infected by feeding on Hosts 21 and 22. The infection may have originated in the larvae of a previous generation feeding on another host species.

The evidence presented above establishes the recovery of *R. orientalis* from *Trombicula fletcheri* and indicates that this species of trombiculid mite serves as a vector of tsutsugamushi disease in northeast New Guinea.

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AGGLUTINATION OF STAPHYLOCOCCUS AUREUS IN THE PRESENCE OF CHORIO-ALLANTOIC FLUID FROM HEN'S EGGS[1, 2]

CERTAIN strains of *Staphylococcus aureus* will agglutinate when grown in the presence of normal[3] or influenza (PR8) virus-infected chorio-allantoic fluid. However, egg fluids vary in their ability to manifest this phenomenon, as is shown by the fact that a clumping of bacteria will occur in a dilution of 1 to 64 with some fluids and only 1 to 4 with others. Moreover, various strains of staphylococci, when cultured in the same chorio-allantoic fluid, may differ in their ability to show agglutination. Therefore it appears that there are two principal variables involved in the manifestation of this reaction, one associated with the organism, determining whether it will or will not be refractory, the other present in the fluid, determining whether or not it will exhibit the effect.

The phenomenon may be demonstrated by adding a drop of a six- to eight-hour nutrient broth culture of susceptible *Staphylococcus aureus* to varying dilutions, in extract broth, of normal or virus-infected chorio-allantoic fluid. These cultures are then incubated over-night at 37° C. and observed the following morning after being held at room temperature for an hour. Readings are made on a rough quantitative scale in a manner similar to that used in the conventional agglutination test, assigning values ranging from 1+ to 4+.

A wide variety of bacteria, including Gram-positive and negative cocci and rods, have been tested, but of those investigated only certain strains of *Staphylococcus aureus* and possibly *Staphylococcus albus* definitely participate in the reaction. *Staphylococcus citreus*, tested a few times, has been consistently refractory. The phenomenon may be elicited by using heat-killed staphylococci or living bacteria. While the agglutination takes place in a higher dilution of egg fluid when killed organisms are used, the clumps formed are usually smaller and the extent of reaction from tube to tube may vary irregularly. All the present observations were made with living bacteria.

Of the 31 cultures of *Staphylococcus aureus* studied, including 26 freshly isolated strains from human sources, two of animal origin and three laboratory strains, 10 of the human pathogens and one of the laboratory cultures were clumped when grown in egg fluids. While most of the agglutinable strains give an occasional negative reaction, those bacteria which are refractory are consistently so. The most outstanding example of the latter is the Wood 46 strain. On the other hand, a freshly isolated strain of staphylococcus, designated as "Craig," has always agglutinated in the presence of egg fluids infected with influenza virus and practically always with normal fluids. These two strains, therefore, have been used to evaluate the relative potencies of various chorio-allantoic fluids. Of 106 tests run with the Craig strain against normal fluid, only 11 failed to yield clumping. Of the 48 tests carried out with Craig and the virus-infected fluids, all showed agglutination. The Wood 46 strain has never shown agglutination with either normal (43 tests) or virus-infected (81 tests) egg fluids.

The agglutination of susceptible bacteria by chorio-allantoic fluid is not limited to any one medium in which the organisms may grow. All the media tried—extract broth, infusion broth, "Savita" and peptone broth—support the phenomenon. Everything else being equal, the extent of agglutination in these various media appears to depend upon the degree of growth or the number of the organisms present. However, there is one exception to this generalization, in that for some reason yet to be determined, susceptible staphylococci growing in a medium of vitamin-free casein digest, nicotinic acid, thiamin, biotin and salts are completely refractory to the effect of all chorio-allantoic fluids, normal and virus-infected.

It does not matter so far as the qualitative aspects of the test are concerned whether the staphylococcus-egg-fluid mixtures are incubated at 37° C. or at room temperature. If the growth is too heavy, the test may prove difficult to interpret. Most of the tests have been run at an original pH of 7.3, which may be reduced to around 6.8 after 18 hours' incubation. However, further studies have shown that the reaction

[1] Preliminary studies.

[2] This investigation is aided by grants from the Fluid Research Funds, Yale University School of Medicine, and the International Cancer Research Foundation.

[3] The term "normal" as used in this paper with reference to chorio-allantoic fluid and mouse lung filtrates is in contrast to the influenza-infected materials. It does not imply that these "normal" substances may not possess other anomalous agents which may support this agglutination phenomenon.

is favored by more alkaline pH. Changes in surface tension of the media[4] do not alter the manifestation of agglutination by susceptible bacteria so long as growth is possible.

No correlation has been found between agglutinability of susceptible organisms and their capacity to produce coagulase, to ferment mannitol and to produce rabbit-cell hemolysin. Agglutinable staphylococci have been tested with other materials from the egg, such as albumin, yolk and an emulsion of chick embryo, but none has given the phenomenon as described. A limited number of observations suggest that amniotic fluid probably possesses, in common with the chorio-allantoic fluid, the ability to exhibit the reaction. The effects of normal horse serum as well as peptone have been tested with negative results. Further, there is no apparent relation between the present agglutination reaction and the known property of some staphylococci to show clumping when grown in media containing human red blood cells. Experiments have ruled out the possibility that this reaction is associated with any colony change due to bacterial dissociation. Preliminary observations suggest that bacteriophage[5] does not play a role in this phenomenon, since both the Craig and the Wood 46 strains have been shown to carry bacteriophage.

This property of the egg fluid, whether in normal or virus-infected material, disappears very rapidly (in 1 to 2 min.) at 56° C. If, however, the titer is unusually high, exposure for 5 minutes at this temperature may be required for inactivation. The agglutinating property of the fluid will remain active at ice-box temperature for a month or more.

When this agglutination phenomenon was first observed, it was in association with influenza virus-infected chorio-allantoic fluid. However, some normal fluids were soon found to manifest the same effect with susceptible bacteria. In these early experiments filtrates[6] of mouse lung infected with influenza virus were tested as well as filtrates from normal mouse lungs. Similar results were obtained using these reagents as have been described for the chorio-allantoic fluids. Wood 46 strain showed no agglutination with virus-infected or normal lung filtrates in the tests made, 14 and 12, respectively. The Craig strain was agglutinated by all 14 virus-infected filtrates, but in only 4 of the 12 tests with normal lung material did the reaction take place. This aspect of the work while interesting has not been stressed, for when filtrate-broth mixtures stand for 18 hours at 37° C. or at room temperature, the precipitation of denatured proteins makes reading of the test difficult. While most samples from normal lungs tested against various strains of staphylococci gave negative reactions (27 tests), occasionally positive results were obtained (4 tests). Agglutinins for staphylococci were lacking in the blood serum from these mice.

Just what part, if any, the influenza virus plays in this agglutination is not understood at present. The fact that most normal chorio-allantoic fluids give the reaction would tend to minimize the importance of this infecting agent. Also, recent experiments show that if one adsorbs the influenza virus from infected fluids with chicken red blood cells and elutes the virus in buffer,[7] the fluid which no longer gives the agglutination of red blood cells agglutinates susceptible staphylococci to the same titer as before adsorption. On the other hand, the buffer into which the virus is eluted does not possess the ability to agglutinate susceptible bacteria even though the virus has been concentrated, as shown by the chicken red blood cell agglutination test.

Summary: Certain strains of *Staphylococcus aureus* will agglutinate when grown in the presence of normal or influenza virus-infected chorio-allantoic fluid. Fluids are rendered inactive after heating at 56° C. for one or two minutes. Surface tension and temperature are not important factors in the manifestation of the phenomenon so long as they are within the limits compatible with growth. The reaction is favored by an alkaline pH. Bacterial dissociation is not a feature of this phenomenon and the relationship of this reaction to bacteriophagy is probably not significant but is being investigated further. Similar reactions as described for the egg fluids may be seen when Berkefeld filtrates of influenza virus-infected and normal mouse lungs are used. A more detailed account of all the data will appear at a later date.

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AN ANTIGEN-ANTIBODY REACTION WITH TETRAHYMENA WHICH RESULTS IN DYSTOMY[1]

AN interesting reaction of the free-living, holotrichous ciliate, Tetrahymena[2] (Colpidium-Glaucoma group), has been observed in experiments dealing with several strains of the organism and immune rabbit sera. These ciliates show the agglutinative, paralytic and sheath-formation reactions described by Robertson[3] when they are incubated for an hour or

[4] W. E. Larson, W. F. Cantwell and T. B. Hartzell, *Jour. Infect. Dis.*, 25: 41–46, 1919.

[5] F. d'Herelle, "The Bacteriophage and Its Behavior," p. 73. Baltimore: Williams and Wilkins, 1926.

[6] Mouse lungs, both normal as well as virus-infected, were ground and filtered through a Berkefeld "N" filter before use in the test.

[7] W. M. Stanley, *Jour. Exp. Med.*, 79: 255–65, 1944.

[1] This work was aided by a grant from the Rockefeller Foundation.

[2] We are very grateful to Professor George W. Kidder for the cultures used in this work.

two in mixture with antisera of appropriate dilutions. In still higher dilutions and with further incubation they show a sharp increase in the number of cells in division as compared to the number of young and mature cells not in division. In some experiments as many as 80 per cent. of all the cells used in the test have been found in division at one time. With continued incubation, running up to 24 hours, many of the pairs of cells which seem unable to complete the process of division have been seen to undergo further abortive attempts at division and develop into chains of three or four parts or into multinucleated giant cells of very irregular shape.

The reaction seems to be an antigen-antibody affair: it has been observed in all combinations of organisms and antisera in which the reactions described by Robertson occur; it has not been observed in combinations with antisera or normal serum in which those reactions do not occur. Table 1 illustrates the specificity of the reaction and the frequence with which it occurs in populations subjected to antibody.

We have been impressed with the ability of these organisms to continue growth in spite of a sharp delay or failure to complete division when under the influence of antibody. The rate of increase of total sedimentable cell volume, as measured in Goetz phosphorous tubes in several experiments, seemed to be about the same in the presence of dilute but effective antibody as in normal control serum. Moreover, the progressive increase in size of many affected cells has been followed microscopically. Thus the principal involvement of the organisms in the reaction seems to be connected with the cell surface.

It is perhaps especially significant that other cultures of this genus have been reported by Chatton and Chatton[4] and Sonneborn[5] to exhibit somewhat similar phenomena when grown in the presence of certain selected strains of bacteria. In both of these studies the occurrence of an increased number of dividing pairs of organisms and the development of monsters was recorded, but there seems to be some difference in the details of events they observed and the reaction recorded here.

TABLE 1

THE REACTIONS OF TETRAHYMENA, STRAIN H, IN SELECTED ANTISERA

Type	Rabbit Serum Dilution 1–16	1–32	1–64	1–128	1–256	1–512	1–1024	Reaction
homologous immune	++++	++++	++	+	–	–	–	Agglutination
	++++	++++	+++	++	+	–	–	Immobilization
	0	5	15	64	36	10	2	Dividing pairs (1)
	68	55	38	17	12	57	48	Single individuals (2)
	0	0.10	0.40	3.80	3.00	0.20	0.04	Ratio (1) to (2)
heterologous immune	–	–	–	–	–	–	–	Agglutination
	–	–	–	–	–	–	–	Immobilization
	2	8	1	2	7	4	4	Dividing pairs (1)
	38	44	62	39	75	75	52	Single individuals (2)
	0.05	0.20	0.01	0.05	0.10	0.05	0.08	Ratio (1) to (2)
normal	–	–	–	–	–	–	–	Agglutination
	–	–	–	–	–	–	–	Immobilization
	4	4	2	2	3	2	3	Dividing pairs (1)
	52	60	43	48	30	62	50	Single individuals (2)
	0.08	0.06	0.05	0.04	0.10	0.03	0.06	Ratio (1) to (2)

Legend: ++++ to +, strong to weak reaction; – no reaction.

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ORAL ADMINISTRATION OF PENICILLIN IN CORN OIL AND LANOLIN

PREPARATIONS for oral administration of penicillin are undoubtedly increasingly in demand. Since Libby's[1] original demonstration that appreciable concentrations of penicillin can be attained in the animal body following the oral administration of penicillin in cottonseed oil, a number of modifications have been offered by other investigators with varying results.

György *et al.*[2] have given penicillin orally with trisodium citrate as a buffer salt to eliminate the destructive action of the hydrochloric acid in the stomach. Chow and McKee[3] delayed the action of penicillin by combining it with human plasma proteins. Little and Lumb[4] report results with a combination of the stabilizing effect of protein and the buffer action of sodium bicarbonate. Their best results were obtained with using raw egg as the protein. The work of Charney,

[3] M. Robertson, *Jour. Path. and Bact.*, 48: 305, 1939.

[4] E. Chatton and Mme. Chatton, *Rev. Suisse de Zool.*, 32: 99, 1925.

[5] T. M. Sonneborn, *Biol. Bull.*, 43: 187, 1932.

[1] R. L. Libby, SCIENCE, 101: 178, 1945.

[2] P. György, H. N. Vandergrift, Wm. Elias, L. G. Colio, F. M. Barry and J. D. Pilcher, *Jour. Am. Med. Asn.*, 127: 639, 1945.

[3] B. F. Chow and C. M. McKee, SCIENCE, 101: 67, 1945.

[4] C. J. Harwood Little and George Lumb, *Lancet*, 1: 203, 1945.

Alburn and Bernhart,[5] using the gastric antacid trisodium citrate, demonstrates that such neutralization of the gastric acidity permits the absorption of a significant quantity of penicillin by the oral route of administration.

In order to protect the penicillin from the gastric acidity and thus make it available for absorption from the small intestines, where most of the fat digestion occurs, we combined a light oil with a heavier greasy substance (lanolin) and found that in this way the absorption period could be materially extended. The lanolin is also instrumental in providing a uniform and stable suspension.

PREPARATION OF PENICILLIN SUSPENSION

Ingredients:

Anhydrous Lanolin U.S.P.	50 per cent.
Corn Oil (Edible grade)	50 " "
Penicillin calcium	q.d.

Weigh the lanolin and corn oil in a suitable container and heat gently to 55–60° C. Mix well in a Micro-mincer[6] until homogeneous. Allow to cool to about 40° C, at which point incorporate the penicillin. Mix thoroughly and dispense in No. 1 gelatin capsules (55,000 Oxford units per capsule).

EXPERIMENTAL

One capsule was taken by each subject at 7:00 A.M., following an overnight fast. No food or liquid was allowed for a minimum of two hours after the dose was taken. Each urinary excretion was collected during a period of 48 hours, the volume recorded and an aliquot placed in a bottle containing ether and phosphate buffer for preservation until assayed. The assay of penicillin was performed by the Rammelkamp method.[7]

RESULTS

Urine concentrations of penicillin which were attained at the various time intervals are recorded in Fig. 1. The penicillin levels in the control subjects who received their dose of penicillin in normal saline solution are presented for comparison.

The average total recovery of penicillin in human urine in the vehicle described was 14 to 16 per cent. in the 24-hour period. The average total recovery of penicillin in the control subjects taking the penicillin saline combination was 2 to 3 per cent. under the same test conditions.

Previous investigations disclose measurable urinary excretions of penicillin following oral administration up to 6 to 12 hours.[1, 4, 5]

[5] J. Charney, H. E. Alburn and F. W. Bernhart, SCIENCE, 101: 251, 1945.

[6] W. C. Alford and E. D. Palmes, *Jour. Lab. Clin. Med.*, 29: 1104, 1944.

[7] C. H. Rammelkamp, *Proc. Soc. Exp. Biol. and Med.*, 51: 95, 1942.

In a group (I) of individuals (predominately males) as shown in Fig. 1 (A) the highest level of penicillin appears in the urine in approximately 2 hours; whereas in another group (II) of individuals

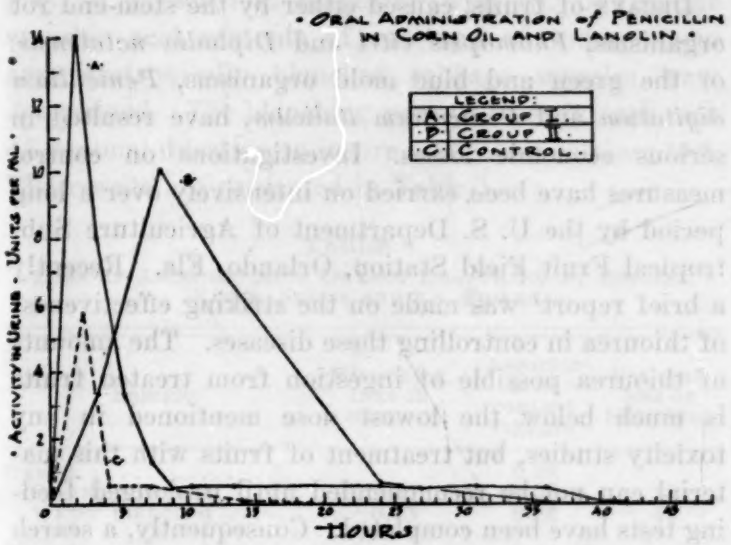

FIG. 1

(predominately females) as shown in Fig. 1 (B) the highest level of penicillin does not appear in the urine until after approximately 8 hours. No explanation for this difference is advanced.

The combination of penicillin in corn oil and lanolin here reported was found in human urine in measurable quantities for 24 hours and in some individuals for more than 42 hours. The prolonged absorption of the penicillin may be attributed to the additive value of both ingredients. The degradation of the corn oil undoubtedly does not occur under the acidic condition of the stomach but rather in the small intestines.[1] The lanolin is chiefly composed of the esters of higher alcohols (cholesterol and isocholesterol) which are by their nature very difficult to decompose. This has the distinct advantage of further delaying the absorption.

SUMMARY

Oral administration of penicillin suspended in equal parts of corn oil and lanolin extends the maintenance of the penicillin level in the system (as determined by urine bio-assay). Measurable quantities were found 24 to 42 hours after ingestion.

Recovery of the penicillin is about five times higher than under administration in saline solution.

We wish to express our sincere appreciation to the various members of our staff who volunteered as subjects for these experiments.

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SCIENTIFIC APPARATUS AND LABORATORY METHODS

COMPOUNDS FOR CONTROL OF ORANGE DECAYS

DECAYS of fruits, caused either by the stem-end rot organisms, *Phomopsis citri* and *Diplodia natalensis*, or the green and blue mold organisms, *Penicillium digitatum* and *Penicillium italicum*, have resulted in serious economic losses. Investigations on control measures have been carried on intensively over a long period by the U. S. Department of Agriculture Subtropical Fruit Field Station, Orlando, Fla. Recently a brief report[1] was made on the striking effectiveness of thiourea in controlling these diseases. The amounts of thiourea possible of ingestion from treated fruits is much below the lowest dose mentioned in any toxicity studies, but treatment of fruits with this material can not be recommended until prolonged feeding tests have been completed. Consequently, a search has been made for less objectionable compounds of equal effectiveness.

Compounds for testing were selected in part on the basis of structural similarity to thiourea and in part on the basis of reports of promising materials by other workers.[3, 5]

Of twenty-five materials recently tested, thioacetamide, 8-hydroxy=quinoline sulfate and 2-aminothiazole gave good to excellent control of decays. The results obtained with those concentrations found most effective are presented in Table 1.

TABLE 1

CONTROL OF ORANGE DECAYS

Treatment	No. of experiments	No. fruits treated	Decays		
			No. stem-ends	No. penicillium	Per cent. decay
Thioacetamide, 5 per cent. ..	5	232	2	2	1.7
Check	5	231	46	30	32.9
8-Hydroxyquinoline sulfate 5 per cent.	2	86	0	9	10.5
Check	2	86	18	10	32.6
2-Aminothiazole, 5 per cent. (110° F.)	2	80	2	4	7.5
Check	2	83	31	4	42.2

In the experimental treatments oranges were dipped from 2 to 5 seconds in water solutions. Each lot consisted of approximately 40 fruits. Several varieties were used, and in most experiments the fruits had been previously exposed to ethylene gas to predispose them to rapid stem-end decay. After treatment the fruits were held at 70° F. for several weeks before examination.

The explanation for the effectiveness of three of the materials found to date may lie in certain similarities of chemical structure. It appears that the presence of both an amino group and sulfur is essential for fungicidal activity in these compounds. Thiourea, previously reported on, is effective, while urea is ineffective. Both compounds carry amino groups, but the effective one carries in addition divalent sulfur. Thioacetamide (Table 1) is effective, while thioacetic acid is not. In this case both compounds carry sulfur, but the effective one carries in addition an amino group. The compound 2-aminothiazole also satisfies this criterion and is effective (Table 1). Thiourea in water solution is reported to tautomerize to the thiol form;[4] if so, it is probable that thioacetamide and 2-aminothiazole do likewise. Cristol *et al.*[2] maintain, however, that the thiol form does not exist in neutral aqueous solution and that $S=C(NH_2)$ and $HN=C(NH_2)$ are the only possible forms. It is not possible at this time to state whether the toxicity noted in these thio-amino compounds is due to the presence of a thiol form or a ring form.

To the best of our knowledge the compounds studied may also require considerable toxicity investigation before they can be accepted for use in the treatment of fruits. Since, however, they are effective and since it is possible that their toxicity may be of such order that they would be preferable to thiourea, we feel the data concerning their effectiveness should be presented for consideration by those interested in this problem.

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[1] J. F. L. Childs and E. A. Siegler, *Phytopathology*, 34(11): 983–985, 1944.

[2] P. Cristol, R. Seigneurin and J. Fourcade, *Compt. Rend.*, 200: 2223–5, 1935; *Chem. Abst.*, 29: 7159–9, 1935.

[3] W. M. Hoskins, H. P. Bloxham and Marian W. Van Ess, *Jour. Econ. Ent.*, 33(6): 875–881, 1941.

[4] H. Rivier and James Borel, *Helv. Chim.*, Acta II, 1219–1228, 1928.

[5] George A. Zentmyer, *Phytopathology*, 32(1): 20, 1942.

THE ELECTRONIC BLANCHING OF VEGETABLES[1]

FOR their successful preservation by freezing or dehydration, vegetables are briefly exposed to flowing steam or boiling water. This heat treatment results in the inactivation of enzymes which may be respon-

[1] Journal Paper No. 637, of the New York State Agricultural Experiment Station, Cornell University, Geneva, N. Y., June 4, 1945.

sible for the deterioration of flavor and destruction of ascorbic acid and carotene during storage. The use of these heating agencies, however, often damages the texture of the vegetable, making them undesirably soft. Moreover, the steam or boiling water leaches out vitamin C and members of the vitamin B complex from these foodstuffs.

It has occurred to us that if electronic heat could be employed in lieu of steam or boiling water, the texture might be improved and losses in vitamin content due to leaching greatly reduced, if not eliminated. Further, through the use of high frequency electricity it was thought possible to place the washed fresh vegetables in the final retail cartons, pass them through a high frequency field for enzyme inactivation and thence into the freezer. Such a procedure should eliminate much handling and possible attendant contamination of the vegetable before it reached the consumer in the frozen state.

In preliminary experiments frequencies of 7 to 10 and 28 to 29 megacycles were used, but the application of sufficient r.f. power to cause the rapid heating of peas, diced carrots and diced potatoes resulted in arcing between the electrodes and any projecting vegetable tissue. There was also burning between individual pieces, although the tendency to arcing or flashover was less at the higher frequency. Recourse was then made to a frequency of 150 megacycles. Experiments conducted on the heating of cabbage with an oscillator[2] having an output of 750 watts at this high frequency have shown that there is little tendency to arc if the vegetable is tightly packed into the container. In testing the effectiveness of dielectric heating, heads of cabbage were cut into slices an eighth of an inch thick and the shredded material packed into Peters-type cartons commonly used in the freezing of vegetables. A carton of shredded cabbage was placed between two copper electrodes mounted in an electric air oven. Tuning stubs were attached to the electrodes to eliminate standing waves[3] and assist in coupling the load to the oscillator. An oven temperature of 100° C. was used to prevent the condensation of moisture on the electrodes and counteract heat losses from the carton by radiation. A heating period of two to three minutes was sufficient to raise the temperature of 180 grams of cabbage to 99° C., as indicated by a spirit-filled thermometer inserted in the carton.

As an indication of the small nutrient losses that may be expected in blanching with r.f. power, the ascorbic acid contents of raw and of water, steam and electronically blanched cabbage samples were determined. The blanching periods were in each case of minimal duration to insure a negative catalase test. The results are presented in Table 1.

TABLE 1

LOSS OF ASCORBIC ACID DURING BLANCHING BY BOILING WATER, STEAM AND R.F. POWER

Sample	Blanching time in minutes	Ascorbic acid content mg/gm	Per cent. loss on blanching
Raw I		0.38	
Steam blanched	2.5	0.26	32
Water blanched	0.75	0.23	40
Raw II		0.34	
Electronically blanched	2.5	0.33	3

The same lot of shredded cabbage was used for all three blanching operations, and 35-gram portions were taken for analyses to insure adequate sampling. The water and steam treatments were carried on simultaneously, hence only a single analysis of the raw product sufficed as a reference. Since the electronic blanching was performed an hour later and raw shredded cabbage loses ascorbic acid on standing, a second raw sample was analyzed immediately prior to r.f. application.

The nearly negligible loss of ascorbic acid during electronic blanching in contrast to the 30 to 40 per cent. losses occurring in the steam and water processes points the way to production of processed vegetables of higher nutritive value. Other vegetables have been successfully blanched by electronics, and more extensive studies of the value of dielectric heating for the inactivation of enzymes in fruit and vegetables are in progress and will include storage trials.

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[2] We are indebted to R.C.A. for the loan of the oscillator and to Dr. G. H. Brown and Mr. R. A. Bierwirth, of the R.C.A. Laboratories, Princeton, N. J., for their help in the arrangement of the tuning circuit.

[3] R. A. Bierwirth and C. N. Hoyler, *Proc. Inst. Radio Engrs.*, 31: 529–536, 1943.

DISCUSSION

FAGARINE, A POSSIBLE SUBSTITUTE FOR QUINIDINE

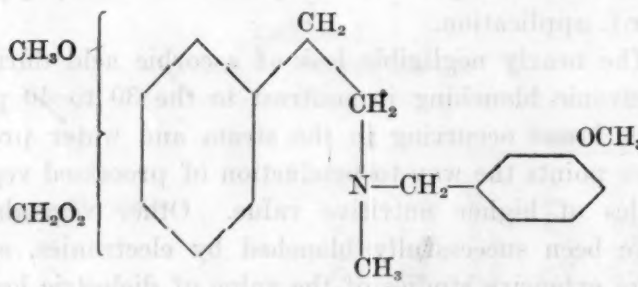
THE present difficulty of obtaining quinidine in quantity has prompted us to send the following information on α-fagarine, which has cardiac effects similar to those of quinidine leading us to believe that it might be employed as a substitute and, more important, that it might open the way for the prepara-

tion of new substances having the same or superior quality as the classical cinchona alkaloid.

Stuckert[1] was the first to isolate some new crystalline bases from the leaves and young twigs of *Fagara coco* (Gill) Engl., a tree growing in central and northern Argentina. He called the three major alkaloids α, β and γ-fagarine. We shall designate the first alkaloid as fagarine only in this article and in future papers, and shall leave the other two names with the Greek initial letters to differentiate them.

Deulofeu, Labriola and De Langhe[2] showed that β-fagarine was identical with skimmianine and that γ-fagarine was a methoxydictamine. It has been finally established that the last base corresponds to 8-methoxydictamine. Details of this work by Berinzaghi, Deulofeu, Labriola and Muruzabal are in course of publication.[3]

Fagarine has a structure different from the other two bases. Deulofeu, Labriola and De Langhe[2] found that it was a stronger base, had two methoxyl groups, one dioxymethylene group and one methylimino group. They proposed the formula $C_{18}H_{21}NO_4$. Deulofeu and Labriola in unpublished experiments have found on the basis of new analyses of the picrate and the methiodide that formula $C_{19}H_{23}NO_4$ agrees better with the analytical data. On oxidation with acid permanganate, fagarine yields m-methoxybenzaldehyde, so that a probable structure could be:



The pharmacological effects of this alkaloid were studied by Stuckert and Sartori,[4] who found in amphibians and rabbits a depressive action on cardiac function. Moisset de Espanés and Moyano Navarro[5] found in dogs a depression of all cardiac fundamental properties. The cronaxie of the myocardium is prolonged.[6]

The threshold for tachysistolia and fibrillation, both auricular and ventricular, to faradic stimulation, is increased, fagarine being more active than quinidine when given in the same doses; besides the spontaneous auricular fibrillation developed in the course of some experiments on the exposed heart rapidly vanished under the effect of fagarine.[7]

Fagarine, as opposed to quinidine tried out under the same conditions, decreased in dogs the risk of primary ventricular fibrillation following experimental coronary occlusion.[8] So far as toxicity is concerned, dogs and rabbits tolerated doses of 5 mg per kilo given endovenously three times a day for 45 days without any actual or subsequent disturbance.[9]

Taquini[10] has tried fagarine with six patients, two with auricular flutter and four with auricular fibrillation. The cases with auricular flutter had a coronary cardiopathy; two out of the four with auricular fibrillation were affected by rheumatic mitral stenosis, and the other two had a coronary cardiopathy. All the cases were studied for a period varying from several weeks to several months before the administration of fagarine. In all of them but one, quinidine administered in the usual dose had failed.

From 0.06 to 0.1 g of fagarine hydrochloride, in water solution, were administered intramuscularly to each patient in a single dose. Within 30 minutes in all cases a normal sinus rhythm was reinitiated. In one of the cases after 28 days the flutter recurred as a consequence of an unusual effort of the patient. A new administration of fagarine was again efficient to reinstall a sinus rhythm.

According to these results we believe that this drug will be successfully employed in the treatment of these and other disturbances of the cardiac rhythm. The detailed clinical observations and the pharmacological effects on man will be published soon.

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[1] G. Stuckert, "Investigaciones del Laboratorio de Química Biológica, Córdoba," Vol. I, 1933. Vol. II, 1938.

[2] V. Deulofeu, R. Labriola and J. De Langhe, *Jour. Am. Chem. Soc.*, 64: 2326, 1942.

[3] B. Berinzaghi, V. Deulofeu, R. Labriola and A. Muruzabal, *Jour. Org. Chem.*, in publication.

[4] G. Stuckert and A. Sartori, *Rev. Univ. Nac. Córdoba, Argentina*, 19, 1932.

[5] E. Moisset de Espanés and B. Moyano Navarro, *Rev. Soc. Arg. Biol.*, 12; 137, 1936; *Comp. rend. Soc. Biol.*, 127: 510, 1938.

[6] E. Moisset de Espanés, *Rev. Soc. Arg. Biol.*, 13: 259, 1937; *Comp. rend. Soc. Biol.*, 126: 834, 1937.

[7] E. Moisset de Espanés, *Rev. Soc. Arg. Biol.*, 13: 112, 1937; *Comp. rend. Soc. Biol.*, 127: 118, 1938.

[8] E. Moisset de Espanés, *Rev. Soc. Arg. Biol.*, 13: 116, 1937; *Comp. rend. Soc. Biol.*, 127: 233, 1938.

[9] E. Moisset de Espanés, *Rev. Soc. Arg. Biol.* 12, 378, 1936; *Comp. rend. Soc. Biol.*, 127: 579, 1938.

[10] A. Taquini. Unpublished results.

THE EFFECTS OF DDT AND OF SODIUM MONOFLUORACETATE UPON PHYSARELLA OBLONGA MORGAN

THE efficacy of DDT as an insecticide has naturally aroused interest as to its possible use as a fungicide. Yet, so far as I am aware, the only published account of experiments dealing with this problem is that of D. O. Morris.[1] Since, for some time, I have been keeping cultures of the slime mold, *Physarella oblonga*, it occurred to me that it would be of interest to test the effect of DDT upon that organism.

About forty tests were made, most of them involving the use of DDT in acetone. DDT is practically insoluble in water, but is soluble in acetone to the extent of 52.5 ± 2.5 gms/l. A saturated solution of acetone was added to the warm agar culture so as to give an emulsion of known concentration. It was found necessary to evaporate the bulk of the acetone, since experiments demonstrated that it is highly toxic to Physarella. The experiment was also tried of growing Physarella upon plates dusted with dry DDT to the extent of about 40 mgs per sq. cm. of surface. The measure of growth was the time required for a 1 sq. cm. plasmodial transplant to cover the entire plate of 63.58 sq. cms.

Results are given in Table 1. These results indicate that: (1) Physarella grows as rapidly upon treated agar as upon that which is untreated, and (2) there is no correlation between rate of growth and the concentration of DDT. There was some indication that dry DDT delays growth, probably for mechanical reasons, but, on the other hand, it was interesting to note that subsequently the growing plasmodium completely covered the layer of dry powder. Likewise, subsequent growth upon the cultures composed of DDT emulsion was as vigorous as upon untreated cultures. Evidently DDT has no very pronounced effect upon *Physarella oblonga*.

TABLE 1

EFFECT OF DDT ON PHYSARELLA

No. of tests	Quantity DDT Treatment	mgs/ml	Average rate of Growth 1 sq. cm. to 63.58 sq. cms.
4	In acetone	105.0	30 hours
4	" "	52.5	32 "
4	" "	26.2	32 "
4	" "	13.1	29 "
4	" "	6.5	27 "
4	" "	3.2	27 "
4	" "	1.6	32 "
4	Dry DDT on surface	40.0	50 "
3	Untreated controls		32 "

For purposes of comparison the effects of sodium monofluoracetate were considered. This substance is readily soluble in water and probably, like the salts of iodo-acetic acid, acts as an enzyme inhibitor. In any case its effect upon Physarella is pronounced. On cultures containing respectively 12.0, 10.5, 9.0, 7.5 and 6.0 mgs/ml, plasmodia developed and survived at least a week. On cultures containing only 0.75 mgs/ml of monofluoracetate, Physarella did fairly well. In no case, however, did the plasmodium spread characteristically over the plate. Instead it wandered about, the "posterior" portion dying out as the opposite margin advanced. The results, in this case, suggest antagonistic effects between the nutrients and toxic substance.

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[1] Jour. Counc. Sci. Indust. Res. Australia, 17, (4): 289–290, 1944.

RELATIONSHIP BETWEEN PATHOGENICITY AND pH TOLERANCE OF MICROORGANISMS

ACCORDING to hypotheses of Leise and James,[1] pathogenicity of bacteria and fungi seems to be related to tolerance for different degrees of pH; it may be possible to differentiate pathogenic from non-pathogenic microorganisms by growth in alkaline broth, and it may be possible to change a virulent microorganism into an avirulent one by an antitryptic agent. While these possibilities may apply to certain bacteria which the authors studied, they do not apply to all. For example, the pathogenic variant form of *Micrococcus tetragenus*[2] grew better in acid medium. The tolerance of other variant forms of the same strain varied in regard to pH, temperature, atmosphere and other circumstances. Changing a favorable environment for one variant of *M. tetragenus* to one unfavorable to it did not necessarily direct variation toward the form best suited to the changed conditions. Variants seemed to appear by chance, and if a variant appeared which found the new environment favorable, life of the strain was continued.

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SLEEVE STOPPERS IN CLOSED SYSTEMS

WE would like to attest the value of a serum bottle stopper and hypodermic syringe for the addition and

[1] J. M. Leise and L. H. James, SCIENCE, 101: 437–438, 1945.

[2] H. A. Reimann, *Jour. Bact.*, 33: 513–523, 1937.

removal of solutions or gases in a closed system, as described in a recent issue of SCIENCE.[1] The device was incorporated in a simple gasometric pipette for the analysis of respiratory gases which has been in use in our laboratory for the past two years and has proved highly satisfactory. This adaptation of a serum bottle stopper was first suggested to me by Lieutenant Colonel F. G. Hall, while working at the Aero-Medical Laboratory at Wright Field. The pipette assembly was described in the *Journal of the Elisha Mitchell Scientific Society*.[2]

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SOCIETIES AND MEETINGS

ANNUAL MEETING OF THE ROYAL SOCIETY OF CANADA

THE meeting of the Royal Society of Canada for 1945 was held at Queen's University, Kingston, from May 20 to May 23, under the chairmanship of the president, J. K. Robertson, professor of physics at Queen's University. In the scientific sections, one hundred and four fellows and half as many guests were in attendance.

New fellows were presented at the first general meeting, including the following in the scientific sections:

Section III (Chemical, Mathematical and Physical Sciences): R. Brauer, E. W. Hewson, O. J. Walker.

Section IV (Geological Sciences): V. J. Okulitch, J. E. Thomson, H. V. Warren.

Section V (Biological Sciences): E. W. Crampton, J. Labarre, W. Leach, C. A. Mitchell, A. W. H. Needler, D. Y. Solandt.

Besides sectional and business meetings, there were two largely attended evening meetings. On the evening of May 21, the society's medals were presented. Professor R. B. Thomson, of the University of Toronto, received the Flavelle Medal as a tribute to his work on the comparative anatomy and physiology of plants. The Henry Marshal Tory Medal was presented to Professor Otto Maass, of McGill University, who was hailed as a man possessed of experimental skill and scientific imagination, with a fondness for hazardous experiment. Professor Maass is assistant to the president of the National Research Council, director of chemical warfare and smoke for the Department of National Defence, and has played a leading rôle in planning chemical research in Canada since the outbreak of the war. The Willet G. Miller Medal was given to Dr. M. E. Wilson, who, conspicuous among Precambrian geologists of the world, has done much in Canada in guiding, prospecting and encouraging mining. The Lorne Pierce Medal was awarded to L'Abbé Felix Antoine Savard, of Laval University, and the Tyrell Medal to Professor F. Landon, of the University of Western Ontario.

After the presentation of medals, Professor J. K. Robertson delivered his presidential address on the subject, "Continuity and Discontinuity." The paper was divided into two parts, a discussion of the progress of philosophical opinion down to the eighteenth century, followed by an assessment of the emergence of the two conceptions and their development by physicists up to the present day. Recognizing that "present-day physics continues to demonstrate the interplay of continuity and discontinuity," he concludes that "the modern physicist no longer accepts a materialistic philosophy and no longer assumes that, as time goes on, he will learn more and more about the ultimate details of a real objective world. His advances have shown him that measurements and observations can not give him exact knowledge beyond a certain stage, and hence, for him, what is beyond has no meaning. His aim now is the more modest one of describing facts and observations in terms of correlating laws, which in the last analysis can be expressed accurately only by mathematical symbols."

On the evening of May 22, following a complimentary dinner given by the mayor and City Council of Kingston, a popular lecture, "Biological Control of Insect and Plant Pests," was given by Dr. W. R. Thompson, F.R.S., Imperial Parasite Service, Belleville, Ontario. This paper so impressed the fellows that a resolution was passed at a general meeting next day, expressing to the Imperial Institute of Entomology its appreciation of the work done in Canada during the war, and asking that arrangements be made for its continuation.

In Section I, twenty-one papers were presented on subjects of historical or literary interest in French Canada.

In Section II, the presidential address by Professor W. H. Alexander was a provocative discussion of some obvious incompatibilities of temperament as between the ideals of a genuine education and the spirit of the ultrademocratic state as suggested by Plato's Apology to Socrates. Papers were read in the fields of literature, philosophy, history and the social sciences. Anthropology and archeology were represented by papers on "The Distribution of Rubbed Slate Instruments in Eastern Canada" by Dr. Douglas Leechman, and by the myth of "Bear Mother" by Dr.

[1] F. B. Senn, SCIENCE, 101: 392, 1945.

[2] 59: 201–204, 1943.

Marius Barbeau. A timely paper was presented by Professor R. Flenley, "The Results of the Reformation in Germany."

In Section III (chemical, mathematical and physical sciences) the most important feature of the meeting was a symposium on "The Dimensions of the Galaxy." This subject was first treated very ably by Dr. Helen Sawyer Hogg from the standpoint of the observations on globular clusters. Dr. C. S. Beals dealt with the obscuring matter between the stars and its influence on estimates of galactic dimensions. These papers led up to the presidential address by Dr. J. A. Pearce, of the Dominion Astrophysical Observatory, entitled "The Dimensions of the Galaxy as Derived from Studies of Galactic Rotation," in which he reviewed the history of the subject from the time of Herschel to the most recent estimates.

Thirty-five other papers were presented to the section, ten by title. A notable series of ten chemical papers was presented by Professor Paul E. Gagnon, of Laval University, Quebec, ranging from the synthesis of amino acids to the technology of charcoal, and exhibiting the great activity in chemistry at that institution. Professor William Ure, of the University of British Columbia, described the mechanism of the "flotation process" of concentrating ores, showing the necessity of a water-repellent layer on the surface of the mineral. Professor J. K. Robertson, Queen's University, described the effect of high-frequency discharges in producing patterns in thin layers of metal placed in the discharge tube. Five meteorological papers were read by members of the staff of the Meteorological Service of Canada, including a new theory of the mechanism of the "Chinook" wind (the warm dry wind which frequently descends the eastern slope of the Rocky Mountains in Alberta) by D. H. Smith and C. E. Thompson.

Nineteen papers were presented to Section IV. In the presidential address, Dr. J. S. DeLury gave an outline of a hypothesis to explain crustal movements. In his opinion, the earth's crust is strong to a depth of 450 miles or more. Liquid rock, known as magma and as lava when it reaches the surface, is formed in shallow levels by frictional heat generated in crustal movements, and is not inherited from a primitive molten earth. These movements are due to failure in the crust caused by thermal contraction followed by a very protracted process of collapse.

Dr. A. W. Jolliffe presented evidence that geologically the northwestern part of the Canadian Shield may be divided into four subprovinces. From north to south these are: (1) Great Bear—characterized by Proterozoic formations, north-east faulting with right-hand displacements, and U-Ag-Co-Ni-Cu mineralization; (2) Yellowknife—characterized by Archaean formations, north to north-west faulting with left-hand displacements, and Au mineralizations; (3) East Arm—characterized by chiefly Proterozoic formations, north-east faulting, and Cu-Co-Ni-Au mineralization; and (4) Taltson—by both Proterozoic and Archaean formations, north to north-west faulting, and Ag-Pb-Au mineralization.

Dr. T. L. Tanton offered a theory, based on a study of conchilites and the work of W. D. Francis, indicating the steps whereby non-living matter evolved into semi-living organisms that provided the catalyzer for the synthesis of protein and the conditions that induced the evolution of primeval forms of life.

Dr. M. L. Keith described brucite deposits in the Rutherglen District, Ontario. Franco Rasetti reported the discovery of Middle Cambrian fossils in the Gaspé, the first recorded in the Province of Quebec. Dr. R. F. Legget described the geology of the "Shipshaw" area on the Saguenay River, and reported finding wood and other organic matter imbedded in the clay. Peter Ginn described an ultrabasic rock near Lochalsh, Ontario.

Dr. Robert Newton, president of Section V, in discussing "The Northern Limits of Wheat Production," pointed out that wheat production in Canada is mainly confined to the southern plains region of the Prairie Provinces. Its possible northward extension concerns not only the potential world food supply, but also the feasibility of northern settlement. The longer summer days of northern latitudes are favorable to growth, but their value is reduced by association with lower temperatures. Rainfall is another important modifying factor. Moreover, the milling and baking quality of northern wheat is generally inferior. This may not destroy its usefulness as a local food resource, but makes it unsuitable as an article of commerce.

Professor R. B. Thomson, the Flavelle Medal winner, presented an invitation paper entitled, "Food Supply and Budding or Twinning Embryogeny." Professor Thomson believes that the view that the asexual type of embryo initiation involved in budding or twinning embryogeny is due to recent mutation, is not supported by sufficient evidence, whereas that for its being an innate or constitutional potentiality is satisfactory. The expression of this potentiality, however, is generally kept under control as indicated by the prevalence of simple embryogeny (one embryo from one zygote) in the main lines of evolutionary advance. Thus the problem of accounting for the sporadic occurrence of budding or twinning at different levels in such advance is concerned with the elimination of established control.

This has been effected in animals by various physical and chemical experimental procedures. Up to the

present, however, little attention has been given to the influence of food supply, and some experimental and other evidence, particularly the effect of excess nutrition on the production of a free nuclear stage in embryos normally undergoing simple embryogeny, indicates the importance of giving more attention to the possibly broader significance of this factor.

Dr. W. H. Cook, director of the Division of Applied Biology of the National Research Council, discussed some of the war research projects of the council under the title "Some Wartime Food and Supply Problems." Under war conditions the main problem in feeding civilian or service personnel is that of transport and distribution, complicated by the perishability of many foodstuffs. To meet the emergency, facilities had to be improvised to preserve the product, or alternatively the foodstuffs themselves had to be rendered less perishable. The dehydration of foodstuffs rich in proteins and fats was discussed in relation to the measurement and maintenance of quality and the type of deterioration that occurs.

Several new chemicals required by war industry can be provided by the fermentation of starch. Reference was made to the bacterial fermentation yielding 2,3-butanediol, a material readily converted to butadiene and other chemicals.

Thirty-eight other papers on various phases of biological and medical sciences made up the program of Section V. These included an important communication by Dr. B. P. Babkin, describing the interference of quinine bisulphate with cholinergic mechanisms in the heart and stomach of the dog, and a demonstration by Dr. C. C. Macklin that venule capacity in the lung is increased on inspiration.

Officers for 1945–46 were elected as follows: *President,* Professor E. S. Moore, University of Toronto; *Vice-president,* Professor H. A. Innis, University of Toronto; *President, Section I,* Dr. S. Marion, Ottawa; *President, Section II,* Professor D. C. Harvey, Dalhousie University, Halifax; *President, Section III,* Professor C. T. Sullivan, McGill University; *President, Section IV,* Dr. B. R. McKay, Ottawa; *President, Section V,* Dr. B. P. Babkin, McGill University.

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SCIENTIFIC BOOKS

CLIMATE AND HUMAN HEALTH

Climate and the Energy of Nations. By S. F. MARKHAM. x + 236 pp. Illustrated. Oxford University Press. 1944. $3.50.

THE relation of climate to the incidence of infection has attracted interest for a long time, but only recently has the effect of climate on individual fitness received much scientific study. This has resulted to a large extent from the difficulties experienced in maintaining full efficiency in troops exposed to extreme climatic conditions. Consequently, laboratories have been set up for the wartime study of such problems in Germany, Russia, Canada, England and on a particularly large and elaborate scale in this country. A large number of trained personnel exist, and it would be a misfortune if their experience ceases to be utilized for the public good after the war.

The main object of this note is to draw attention to a recent work by S. F. Markham (an English Member of Parliament) entitled "Climate and the Energy of Nations" (Oxford Press, 1944). This book traces the spread of civilization in relation to climate, reviewing history with emphasis on the effects of developments in housing, heating of houses, chimneys, glazed windows, central heating and adequate lighting on the spread of culture to more northern climates, where cold and the long winter nights would otherwise have hindered development. The ideas advanced stem from those of Professor Ellsworth Huntington and are presented in a popular manner. While the author's technical knowledge is open to criticism, so that an abstractor for *Biological Abstracts* reviewed the book with little sympathy, the author sees the problems clearly in broad outlines and presents a point of view, which is of considerable public interest. He maintains that men developing under good conditions will outstrip those living under greater handicaps, and that such environmental factors are more important than minor genetic differences between racial strains. Considering how great are the obstacles to book work imposed by long periods of cold and darkness, biologists are apt to agree with him. If the thermal regulation of houses were limited to heating as it has been in the past, one would expect the main centers of civilization to shift more and more to colder climates. If we were able to understand fully the factors concerned, better conditions should be obtained in regulated houses than are found in any natural climate. Mr. Markham presents evidence that high levels of intelligence are more prevalent in areas where extreme climatic conditions are rare. He argues that such intelligence levels are demonstrated in high standards of public health, of foreign trade and national wealth. The relationship of such factors to external climate, if established, are

of importance not only to scientists but also to statesmen and financiers. There is probably a basis of truth and, if so, in the future such developments are likely to be more or less controllable by proper use of air-conditioning and to depend less and less on the external climate.

Tropical areas now provide an interesting field for study, for the efficiency of control of cold conditions is already highly developed. On the other hand, little has been done to obtain practical methods for the application of air-conditioning under the heavy heat loads and on the enormous scale that would be needed to modify life in the tropics. Yet these areas contain enormous undeveloped sources of wealth, and we would be foolish to assume that control can not possibly be attained. There is little doubt that highly populated areas such as India will not be able to compete in the industrial field with areas in which the climate is more favorable, without the use of sweated labor, unless the factories are air-conditioned. It is also very probable that the output of a factory in such a climate would be still more affected beneficially, if the living quarters of the workers could be cooled. If choice had to be made between cooling a factory or living quarters, the latter is probably the more important. Such projects are at present not even under consideration and might involve changes in the housing and living conditions of whole nations in the tropics, since cooling could be more efficiently attained in large buildings.

Not only should air-conditioning be considered for industrialized areas, it may also prove of value to agriculture. Thus in Brisbane recently 25,000 chickens died in a single unusually hot day from heat stroke. This accident led to experimental work in the University of Queensland under Professor D. H. K. Lee, with the result that limits of tolerance and methods of control (by spraying) are now available. The difficulties of obtaining a good yield of milk from cattle in the tropics is well known, but, surprisingly enough, it is claimed that air-conditioning of a milking barn will more than pay for itself by increasing this yield. Also much work in cross-breeding is required to determine the best strains of cattle and other animals for life in the tropics.

It would appear that innumerable fields for study exist, and that the effects of changes in temperature even for part of the day are not readily predictable. We know little about the agricultural problems, we know almost nothing about the human side. We have no information as to the effect on man of living continuously in cooled houses for generations in areas with a hot external climate.

It is not improbable that cooled houses in a tropical climate, if used consistently for one generation, might modify the whole character of a population. It would certainly not be wise to rely for such information on chance observations, when large-scale experiments could be carried out much more accurately, more cheaply in the long run and probably with the approval of those used as subjects. Such experiments involve mental activity and should be made on man. Data of this type might be expensive to obtain but should pay dividends, possibly very large dividends. All the world would be served, the tropical countries through the more rapid development that would be possible when the facts were known, and countries in more temperate zones by demands on their supplies of mechanical equipment. International cooperation, whether on a limited scale as through the Pan American Union, or preferably on a broader basis, should expedite progress.

These future possibilities are only hinted at by Markham. Prophecies as to the future are left to the reader. However, if people with imagination read Markham's speculations as regards the past and make efforts to speculate as regards the future, it is to be expected that some extremely valuable experiments may materialize.

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AMINO ACIDS AND PROTEINS

Outline of the Amino Acids and Proteins. Melville Sahyun, editor. 251 pages. New York, N. Y.: Reinhold Publishing Corp. 1944. $4.00.

AMONG the major problems in the organic chemistry of natural products, that attracting the keenest interest of investigators is the constitution of proteins. As a consequence, much is currently being printed in the technical journals concerning the chemistry of the amino acids and several publishers of scientific books have recently issued text-books on the subject.

The stated purpose of the volume under review is "to outline in a simple and readable manner the essentials of the chemistry and biochemistry of amino acids and proteins." This it attempts to do in a group of essays by more than a dozen experts; as is unfortunately too frequent in such collections, insufficient effort appears to have been made to coordinate the subject-matter and to maintain a logical balance between the individual chapters. Moreover, several of these essays labor under deficiencies of structural equilibrium within themselves. In the opening chapter, discursive accounts of investigations which led to the characterization of individual amino acids are interspersed with passages intelligible only to the expert. How much information could be extracted from the bare remark that the first synthesis

of glutamic acid was accomplished with levulinic acid as starting material? In the account of Hedin's procedure for the isolation of histidine, no reference is made to the fact that the silver salt is precipitated in one of the steps, nor are the conditions of this precipitation indicated. And an uninformed reader could gain little from the statement that Harington, in his work on thyroxine, "subjected his crystalline product to dismutation and identified each fraction."

The story of the discovery of tryptophane is misleading in one respect, apparently owing to the misinterpretation of a passage, paraphrased from a review article by Vickery and Schmitt, to the effect that as a result of Kühne's researches "indole and tryptophane very early became associated with each other." The identification of indole as a product of the putrefaction of proteins was accomplished by Nencki, and not by Kühne.

In the second chapter, on proteins, accuracy and lucidity are too often sacrificed to impressiveness of utterance. For example, it is here stated that "Those substances that are contained in or produced by bacteria and that engender the production of specific immune bodies are likewise proteins"; the reader has to traverse more than 100 pages before encountering the more correct statement that "many antigens are proteins and most proteins are antigens." In the discussion of amino acids as dipolar ions an unsuspecting student would have difficulty in interpreting the dissociation curves (p. 70) in which zero percentage dissociation is attributed to amino acids in the intermediate zones of pH.

On the other hand, the third chapter, on protein structure, is an admirable exposition of a difficult subject; clearly expressed, logical and well balanced.

Chapter IV, on the hydrolysis of proteins, abounds in detailed, but poorly integrated, information. It also contains obscure passages such as "Some hydrochloric acid is lost during boiling. Alkalies . . . absorb carbon dioxide . . . . Therefore, if one wishes to perform accurate hydrolysis and be in a position to duplicate his own results, it is necessary to express the concentration of acids and alkalies in terms of normality," and is not free of errors like ". . . the ratio $\frac{\alpha\text{-amino N}}{\text{total N}}$ is 100."

The fifth chapter, on the synthesis and isolation of certain amino acids, is more elaborate in treatment than the third, but equally meritorious. It is obviously addressed to advanced students, and shows care in the accentuation of principles and the avoidance of unessential detail.

In the next chapter, on methods of analysis for amino acids and proteins, the treatment in some, but not all, sections approaches that of a manual of analysis; the information here supplied could be of practical value only in conjunction with that obtainable from a standard work like that of Hawk and Bergeim. This chapter concludes with a very brief statement, without theoretical explanation, of the electrophoretic procedure of Tiselius for the separation of plasma proteins, a section on "protein levels in health and disease" and some semi-detailed accounts of analytical methods for the determination of serum proteins.

An excellent, though brief, review of the role of amino acids in immunochemistry, addressed to the trained biochemist, is followed by an equally authoritative essay on amino acids in detoxication, the subject-matter for which is carefully selected, informative and thoughtfully discussed. The organic chemist will accept with some reserve the inferences drawn from the results of physiological balance experiments, which are often open to more than one interpretation. The biochemist sometimes yields, for the sake of simplicity, to the temptation to ascribe only one of several possible courses to a series of metabolic conversions. For example, it is here unequivocally stated that in the formation of a mercapturic acid the acetylation takes place subsequently to the combination of the aromatic group with the sulfur atom. This is no doubt probable, but has not been proved.

The chapters on the metabolism of proteins and amino acids and on the intermediary metabolism of individual amino acids are among the best in the book, and will well repay study by biochemist and organic chemist alike. The very short account of nitrogen equilibrium and the biological value of proteins serves as a stimulating introduction to the subject of the final chapter, amino acids and proteins in nutrition, the presentation of which is conscientious but rather lacking in chemical imagination. This failing is perhaps attributable to the magnitude of the load of published matter which the review has to bear.

An appendix contains a list of titles of U. S. patents issued on amino acids and related organic compounds.

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